8

Invertebrates Mitochondrial Function and Energetic Challenges

Oliviert Martinez-Cruz[1], Arturo Sanchez-Paz[2], Fernando Garcia-Carreño[3], Laura Jimenez-Gutierrez[1], Ma. de los Angeles Navarrete del Toro[3] and Adriana Muhlia-Almazan[1]

[1]*Molecular Biology Laboratory, Centro de Investigacion en Alimentacion y Desarrollo (CIAD), Hermosillo, Sonora,*

[2]*Laboratorio de Sanidad Acuicola, Centro de Investigaciones Biologicas del Noroeste (CIBNOR), Hermosillo, Sonora,*

[3]*Biochemistry Laboratory, Centro de Investigaciones Biologicas del Noroeste (CIBNOR), La Paz, Mexico*

1. Introduction

The term "invertebrate" recalls all animal species lacking a backbone or a bony skeleton. Although "invertebrate" is not a scientific term that encloses a taxonomic rank, this group includes animal species represented by over 30 phyla and it includes the first animals that successfully inhabited the earth, an event that – according to the fossil evidence – dates back to around 600 million years ago. This group is composed of several different phyla, such as annelids, molluscs, sponges, cnidarians, echinoderms, and all species from the phylum Arthropoda – which is the largest among invertebrates and is comprised by insects, arachnids and crustaceans (nearly reaching 1,033,160 species).

Since they appeared for the first time during the Cambrian period, invertebrates have played an important ecological role since they are frequently the key constituents of many trophic chains and they occupy virtually every available ecosystem on Earth, being characterised by notable variations in temperature, oxygen concentrations, food availability and food quality. Also, many species occupy highly specific and important roles in nature as pollinators, parasites or vectors for parasitic diseases affecting human and animal health.

It is clear that the ability of invertebrates to inhabit almost every ecosystem – as well as the diverse array of morphological and behavioural strategies used to obtain nutrients from the environment – is an accurate reflection of the enormous ability of these organisms to solve their most basic energetic requirements. From blood-suckers such as mosquitoes, intestinal nematodes and leeches (hirudin), to small plankton marine feeders such as cnidarians and marine benthic bivalves, all species face changes in food availability throughout their life cycle which affect their energy stores and growth rates (Peck, 2002; Popova-Butler & Dean, 2009). A beautiful example of highly specific energy stores – crucial during invertebrates' life cycle and important to human health – is that of the female mosquito (*Anopheles gambiae*), which usually feeds on sugar to gain energy to fly and to cope with metabolic

requirements; however, anautogenous mosquitoes require the energy resulting from blood digestion in order to produce eggs, and it is during blood sucking that *Plasmodium vivax* (the parasite from infected females) enters into the vertebrate host to produce Malaria, a major health problem around the world (Das et al., 2010).

Large energetic demands during external work are observed throughout the life of several invertebrate species, and a clear example may be found in insect flight, which is considered to be one of the most energetically demanding processes of animal locomotion (Harrison & Roberts, 2000). Besides this, being an aerobic process that requires a permanent oxygen supply and depends upon ATP cellular production, the high energetic cost of flying is related to the frequency of the flight muscles' contraction (Vishnudas & Vigoreaux, 2006). In vertebrate species, the existence of high-energetic molecules in the muscle (phosphocreatine) during its exercise has been well documented (Jubrias et al., 2001); however, in invertebrate species, the presence of phosphagen-kinases that catalyse the synthesis of these high-energetic phosphorylated molecules has not been widely distributed (Ellington & Hines, 1991). The insect flight muscle seems to lack such molecules, but some flying species are able to surpass such energy needs by the proximity of mitochondria to muscle myofibrils, thus facilitating the export of energy rich nucleotides – such as ATP – to myofibrils (Vishnudas & Vigoreaux, 2006).

Some other invertebrate phyla – such as crustaceans – are able to synthesise phosphagens differently from that of vertebrates, like phosphocreatine. Phosphoarginine – a phosphagen of L-arginine found in the tail muscle of shrimp and crabs as well as in the flight muscle of flying insects – is the chemical energy storage system of these tissues, and thus animals are able to rapidly produce ATP when it is required (Wegener, 1996; Kotlyar et al., 2000). The enzyme responsible for the synthesis of phosphoarginine from ATP and L-arginine in invertebrates is named 'arginine kinase' and it is also considered to be a major allergen protein for shrimp-allergic individuals (Garcia-Orozco et al., 2007).

Since energetics are considered to be a key factor in limiting organisms' adaptation to extreme temperatures, several invertebrate species inhabiting marine polar environments are known to show a remarkable plasticity as regards their cellular system. Such adaptations may include an increasing number of mitochondria per cell as the temperature decreases as well as differences in the mitochondrial characteristics relating to the species' lifestyle, from motile species to sedentary ones (Peck, 2002). Studies in the mitochondrial function of the eurythermal polychaete *Arenicola marina* have concluded that invertebrates inhabiting higher latitudes – and consequently exposed to cold temperatures – showed higher oxygen consumption, mitochondrial densities and mitochondrial capacities when compared with those organisms living at lower latitudes with higher temperatures (Sommer & Portner, 1999; Peck, 2002). This adaptation of cold-acclimatised organisms is thought to occur in order to equate the level of metabolic activity present at warmer temperatures.

Among other important environmental factors affecting the bioenergetic state of organisms, marine invertebrates face large daily fluctuations in the dissolved oxygen concentrations of water, as well as wide salinity changes between open ocean and coastal waters - where many species live at least during one specific stage of their life cycle - (Dall et al., 1990). Such variations can adversely affect some species whose physiological mechanisms usually do not allow them to cope with low oxygen levels (as oxyregulators) or to handle salinity changes (as osmoregulators). However, several species are able to swim or move from one place to other, searching for a suitable site to grow, reproduce and survive (Hochachka &

Somero, 2002; Abele et al., 2007). Nevertheless, other invertebrate species are highly adapted to live in extreme conditions such as those living in hypoxic or even anoxic environments, like the brine shrimp *Artemia franciscana* (Eads & Hand, 1999; 2003).

As has previously been stated, this chapter reviews the current state of knowledge of the mitochondrial function of invertebrate species. It asks two central questions: 1) How are invertebrates able to adapt to such diverse environmental conditions by using a common set of structures and mechanisms – their mitochondrial machinery – to fulfil their energy requirements along their entire life cycle? 2) Is it really important to understand the role of mitochondria in the life history of invertebrates? This chapter also includes original data on crustacean responses to the external factors affecting such mitochondrial functions as hypoxia, starvation and the energetically expensive molt cycle.

2. The highly conserved mitochondrial machinery of invertebrates: Same functions, different challenges

Following the endosymbiotic origin from primitive bacteria – at least 2 billion years ago – when atmospheric oxygen levels rose and subsequently remained relatively steady, mitochondria have experienced large changes among species, from α-proteobacteria to mammals. During the adaptation process of organisms to their new dynamic environment, some mitochondrial characteristics have remained highly conserved even among distantly related species, such as their rod shape - the overall structure including two phospholipid membranes – and, with some exceptions, their conserved characteristic genome content of 22 tRNAs, 2 rRNAs, and 13 genes encoding protein subunits of the enzymes from the oxidative phosphorylation system (OXPHOS) (Boore, 1999; Gray et al., 1999).

Besides mitochondrial encoded proteins, a significant fraction of the original mitochondrial genes have moved to the nucleus. Thus, in the mammalian mitochondria, approximately 76 subunits – which are part of the respiratory chain – are encoded by nuclear genes, and all of them must be imported into the mitochondria. The complete protein machinery involved in mtDNA replication, transcription and translation (including all of the ribosomal protein subunits) is encoded by nuclear genes (St. John et al., 2005; Falkenberg et al., 2005). Furthermore, several of these imported proteins are highly conserved among species, some of them accomplishing key roles as subunits alpha and beta of the ATP-synthase, which are part of the catalytic sites of the enzyme (Martinez-Cruz et al., 2011).

In addition to those key proteins that maintain a conserved function, hundreds of new proteins have been described among invertebrate species as being imported to mitochondria, each presumed to participate in at least one of the large number of metabolic pathways occurring in this organelle. However, its major conserved function allows mitochondrion to produce – from food assimilated compounds via oxidation – the proton motive force that drives ATP synthesis (Rich & Marechal, 2010). This complex process produces 95% of the cellular ATP that cells need for biosynthesis, transport and motility (Wilson et al., 1988; Dudkina et al., 2008; Diaz, 2010), and any significant change in the system could result in deleterious consequences for the whole cell metabolism and – consequently – reduce its efficiency or provoke its death (Mayevsky & Rogatsky, 2007).

Throughout the years (and mostly based in the study of human pathologies) researchers have found that mitochondria are involved in various critical functions – such as thermoregulation – in the synthesis of essential molecules – such as phospholipids and heme – in the programmed cell death or apoptosis of mediating multiple cellular signalling

pathways (Ryan & Hoogenraad, 2007). Mitochondria are also essential in the cholesterol metabolism and the detoxification of ammonia in the urea cycle. In addition, there is a close relationship between mitochondria and different cell types. It is well known that the number of mitochondria in individual cell types varies according to their function and energy requirements (St. John et al., 2005; Chen & Chan, 2009). Thus, highly energetic tissues as the flight muscle of flying insects and the midgut gland of crustaceans are known to contain a large number of mitochondria, just as occurs in the skeletal muscles of vertebrates during endurance training (Harrison & Roberts, 2000).

Mitochondria are known as dynamic organelles that cannot be made *de novo*, and instead they divide through a highly regulated process called mitochondrial fission, mediated by a defined set of new proteins recruited from the cytoplasm, which are added to pre-existing sub-compartments and protein complexes to a point whereby the organelle grows and divides (Ryan & Hoogenraad, 2007). Furthermore, mitochondria are now seen as a set of organelles that are able to migrate throughout the cell, to fuse and divide regulating mitochondrial function (Chen & Chan, 2009).

Recent findings have also confirmed the existence of dynamic mitochondrial supercomplexes – defined as the association of protein complexes distributed along the inner mitochondrial membrane – on mammals, plants, yeasts (*Yarrowia lipolytica)*, and bacteria (Nübel et al., 2009; Wittig & Schägger, 2009; Dudkina et al., 2010). Complexes I, III and IV are able to associate in order to promote electron transport as single OXPHOS complexes or else as a supercomplex called respirasome ($I + III_2 + IV_{1\text{-}2}$) both of which can autonomously carry out respiration (Wittig et al., 2006). Furthermore, complex V – the mitochondrial F_1F_OATP-synthase – is associated to form dimeric, trimeric and tetrameric organisations (Dudkina et al., 2008). Unfortunately, to our knowledge, there are no reports confirming the existence of these mitochondrial protein associations from invertebrate species.

A general description of the most recent advances covering mitochondrial enzymes participating in the electron transport chain and the OXPHOS, including some particular findings on the enzymes of some invertebrate species, is presented below:

2.1 Complex I, NADH: Ubiquinone-oxidoreductase (EC. 1.6.5.3)

Is an enzyme which provides the input to the respiratory chain by catalysing the transfer of two electrons from NADH from - glycolysis - to ubiquinone, and which utilises the free energy released in this redox reaction for the translocation of four protons across the membrane, from the matrix to the intermembrane space. The proton translocation from the mitochondrial matrix generates the proton-motive force required for ATP synthesis at the end of the respiratory chain during oxidative phosphorylation (Friedrich & Weiss, 1997; Dudkina et al., 2008). However, this proton-pumping enzyme is the largest, most complicated and least-well understood of the respiratory chain (Zickermann et al., 2008). Another unconventional function of complex I is the generation of reactive oxygen species (ROS) – such as the superoxide ion (O_2^-) – and, even if it is not a strong oxidant, it is a precursor of most other ROS and, consequently, contributes significantly to cellular oxidative stress. In mammalian mitochondria, the superoxide production is predominantly produced by complex I (Turrens, 2003).

The scarce information available concerning mitochondrial complex I from invertebrates includes basic descriptive reports of the nucleotide sequences of the NADH subunits - most

of them from the mitochondrial genome-, their proteins, and an interesting study of site-directed mutagenesis aiming to understand the subunits' function in model insect species such as *Drosophila spp*. (Tovoinen et al., 2001; Sanz et al., 2010).

In addition, the existence of an alternative oxidase (AOX) in the animal mitochondria has been confirmed. Previously, this enzyme – which catalyses the O_2-dependent oxidation of ubiquinol, producing ubiquinone and H_2O – was thought to be limited to plants, some fungi and protists. The major difference between complex I and AOX is that the electron flow from ubiquinol to AOX is not coupled to the generation of a proton motive force, decreasing energy conservation in oxidative phosphorylation. The complementary DNA sequence that encodes AOX in invertebrate species from the phyla Porifera, Cnidaria, Nematoda, Anellida, Mollusca, and Echinodermata, has been characterised and it has been suggested that it may contribute on the acclimation of animals to stress conditions, mainly when the cytochrome pathway is inhibited (McDonald et al., 2009).

2.2 Complex II, Succinate: Ubiquinone- Oxidoreductase (EC 1.3.99.1)

Also called Succinate Dehydrogenase (SDH), is a functional member of the Krebs cycle and the aerobic respiratory chain, and it couples the oxidation of succinate to fumarate with the reduction of quinone to quinol (QH_2). Most probably, this enzyme presents the most striking differences among the mitochondrial complexes in the electron transport chain and OXPHOS (Rich & Marechal, 2010). It must be noticed that the oxidation of succinate to fumarate is the only Krebs reaction that takes place in the mitochondrial inner membrane itself; this reaction does not participate in proton translocation from one side to the other of the inner mitochondrial membrane. The energy carrier flavin adenine dinucleotide (FAD) forms a part of complex II, and succinate oxidation begins after the binding of succinate to the enzyme. This covalent binding of FAD to the enzyme increases the redox potential to a level that allows succinate oxidation (Rich & Marechal, 2010).

Contrary to the four human and yeast mitochondrial complexes, which include subunits that are encoded by the mitochondrial genome, the four subunits of SDH are encoded in the nuclear genome (SDH1 to SDH4; Figueroa et al., 2002).

Early studies of complex II (SDH) from invertebrates reported the isolation of mitochondrial fractions from the body muscles of the worm *Nereis virens* and from the tail muscle of the lobster *Homarus gammarus*, and reported high activity in both enzymes (Mattisson, 1965). Unfortunately, there is scarce new information available concerning complex II in invertebrates. However, the study of mitochondria from parasite species – used as animal models – can be considered a framework that has guided our knowledge in the understanding of such critical endogenous processes as aging, mitochondrial dysfunction and the role of the organelle in apoptosis (Grad et al., 2008; Wang & Youle, 2009). Thus, it has been suggested that mitochondria may influence the longevity of the nematode *Caenorhabditis elegans* through the rate of ROS production and by the stress-evoked signals that are known to act in a cell-non-autonomous manner during mitochondrial protein regulation (Durieux et al., 2011). Furthermore, *C. elegans* has been used as a model to investigate the mitochondrial mechanisms of human aging and tumourigenesis by studying the catalytic effects of mutation in the genes encoding the SDH iron-sulphur subunit. Promising results suggest that the SDH ubiquinone-binding site can become a source of superoxide and that the pathological consequences of SDH mutations can be diminished with antioxidants, such as ascorbate and N-acetyl-l-cysteine (Huang & Lemire, 2009).

2.3 Complex III, Ubiquinol: Cytochrome C Oxidoreductase or Cytochrome BC_1 (EC 1.10.2.2)

Is a multimeric enzyme complex involved in the transfer of electrons from ubiquinol to cytochrome C, and it is also coupled to electrons' transfer across the inner mitochondrial membrane. This bovine enzyme is formed by 10 nuclear encoded subunits, with only one encoded in the mtDNA (Xia et al., 1997). The catalytic mechanism of the enzyme includes the complex mechanism of the protonmotive Q-cycle that provides the additional efficiency of the energy conservation of the electrons transferred (Mitchell, 1976; Rich & Marechal, 2010).

In such species as mammals and yeasts it has been observed that as the rate of electron transfer is reduced, the enzyme may leak electrons to molecular oxygen, promoting the formation of the superoxide ion. This mitochondrial dysfunction has been widely studied, and its role in the O_2 sensing pathway has been investigated because the increasing production of reactive oxygen species (ROS) is the result of organisms in hypoxic/anoxic conditions (Guzy et al., 2007). New evidence suggests that ROS generated by the mitochondrial complex III are required for the hypoxic activation of transcription factors such as HIF (Hypoxia Inducible Factor); however, this topic will be more extensively discussed below.

The mitochondrial complex III from invertebrates has been poorly studied, but recent reports about these species confirm the importance of studying its basis and applications. An interesting example is the study about the control of Chagas disease, which severely affects the health of the human population in Latin America and which is caused by the protozoan parasite *Trypanosoma cruzi*. Genes et al. (2011) reported such bacteria species as *Serratia marcescens* biotype A1a, which is regularly found in the gut of the vector insect *Rhodnius prolixus*, and which demonstrates the trypanolytic activity conferred by prodigiosin. Prodigiosin is a potent bacterial tripyrrolic compound with various biological activities. This study suggests the abnormal mitochondrial function of *T. cruzi* since prodigiosin inhibits the mitochondrial complex III, affecting subsequent oxidative phosphorylation.

2.4 Complex IV, Cytochrome C oxidase (EC 1.9.3.1)

Is the terminal enzyme of the electron transport chain and it catalyses the reduction of molecular oxygen to water. The reduction of oxygen by this enzyme – which is responsible for biological energy conversion in mitochondria (Belevich et al., 2010) – is also linked to the translocation (pumping) of four protons across the membrane. This movement of electrons is subsequently coupled to ATP synthesis by the ATP-synthase (Khalimonchuk & Rödel, 2005). The cytochrome C oxidase (CO) has been described as one of the electron transport chain elements which is highly affected by changes in oxygen levels – since cytochrome C reduction is oxygen-dependent – and becomes more reduced when oxygen levels increase (Wilson et al., 1988).

The CO from eukaryotes consists of 11-13 subunits, depending on the species. It belongs to the family of heme-cooper enzymes, some of them suggested as hypoxia sensors. The enzyme is highly regulated by transcription factors, hormones, lipid membranes and the second messengers that control its activity (Ripamonti et al., 2006; Semenza, 2007; Fontanesi et al., 2008). As observed in other mitochondrial complexes, CO also includes mitochondrial encoded genes as subunits CO1, CO2, and CO3 which form the functional core of the enzyme; the rest are nuclear-encoded subunits and their functions – even in the most studied animal models – remain unclear, although they are assumed to participate in the

assembly, stability and regulation of the enzyme (Rich & Marechal, 2010). Moreover, CO is also regulated by the existence of various isoforms from each nuclear-encoded subunit which is known to be tissue- and specie-specific (e. g. CO5a and CO5b, CO6a, CO6b and CO6c, and CO7a, CO7b, CO7c, etc.; Diaz, 2010).

The CO genes' expression and the activity of the enzyme are known to be affected by external factors. In crustacean species, such as the grass shrimp *Palaemonetes pugio*, the gene expression of subunits CO1 and CO2 is positively or negatively regulated by low dissolved oxygen concentrations in water (Brouwer et al., 2008). References and further reading may be available for this article.

In insects, as with the sweet potato hornworm *Agrius convolvuli*, diapause – the delay in development in response to regularly and recurring periods of adverse environmental conditions – is induced by low temperatures. During this physiological state, the neurological activity, oxygen consumption rate and metabolic levels are low compared to undiapause animals; and it has been found that the genetic expression of the CO1 subunit is down-regulated. When the organism terminates diapause, CO1 is up-regulated and the enzyme activity also increases (Uno et al., 2004). Other insect species, such as the cotton boll worm *Helicoverpa armigera*, show diverse responses during diapause: the levels of CO1 mRNA and enzyme activity are low, suggesting that the diapause state is different in each species (Yang et al., 2010).

In some species, CO participates in organism detoxification, as observed in the polychaetes *Hediste diversicolor* and *Marenzelleria viridis* which inhabit eutrophicated regions with low oxygen levels and high sulphide concentrations - where CO functions as an alternative pathway of oxidation - (Hahlbeck et al., 2000). In addition, when sulphide becomes hydrogen sulphide (HS) – a weak acid that occurs in marine and aquatic environments such as hydrothermal vents, mudflats and marshes – HS is known to reversibly inhibit CO activity, affecting the aerobic metabolism of certain species, such as the worm *Urechis caupo* (Julian et al., 1998).

2.5 Complex V, ATP synthase (EC 3.6.3.14)

Is a multimeric enzyme that transforms the kinetic energy of the protons' electrochemical gradient to synthesise the high energy phosphate molecule ATP. Nowadays, it is well-known that the enzyme can also hydrolyse ATP, functioning as an ATPase (Boyer, 1997; Tuena de Gomez-Poyou et al., 1999). This mitochondrial enzyme comprises a catalytic sector F_1 (composed by $\alpha_3\beta_3\gamma\delta\varepsilon$ subunits), and a transmembrane hydrophobic sector F_O (composed of at least three subunits: a, b_2 and $c_{10\text{-}12}$), both linked by a central and a peripheral stalk (Mueller et al., 2004). As in other mitochondrial complexes, this enzyme includes subunits encoded in both the nuclear and mitochondrial genomes, in a tightly coordinated process to assemble this multimeric complex (Itoi et al., 2003; Muhlia-Almazan et al., 2008).

During the oxidative phosphorylation process in mitochondria, the electron transport chain generates a proton gradient that is proposed to drive the rotation of Fo, a central rotor located in the inner mitochondrial membrane. This rotation movement is believed to reverse the rotation of the F_1 nanomotor, inducing – via a conformational change – the sequential release of ATP from three identical catalytic sites followed by the sequential synthesis of newly formed ATP from Pi +ADP at these sites (Cardol et al., 2005). Biochemical and structural studies of the F_1 sector from bovine enzymes have demonstrated that catalytic sites are integrated mainly by three β subunits that alternate with three α subunits. The

three catalytic sites formed by these three pairs of α/β subunits are grouped in segments forming a sphere, which is connected to the γ subunit which connects F_1 to Fo (Lai-Zhang & Mueller, 2000).

Due to its complex structure and the dual role that the ATP synthase plays in cells, the current state of research concerning this mitochondrial enzyme is both abundant and relevant; however, for the majority of invertebrate taxa, the information regarding this enzyme appears to be almost non-existent, restricted to some insect species for the more studied models. Analyses of the mitochondrial transcriptome and proteome from these species – which have been exposed to different environmental conditions – have shown that the ATP-synthase subunits can be affected in their expression, and that specific subunits of this multimeric complex can also play additional roles in the mitochondrial function. These findings suggest that invertebrates are able to respond by changing their metabolism to maintain cell homeostasis.

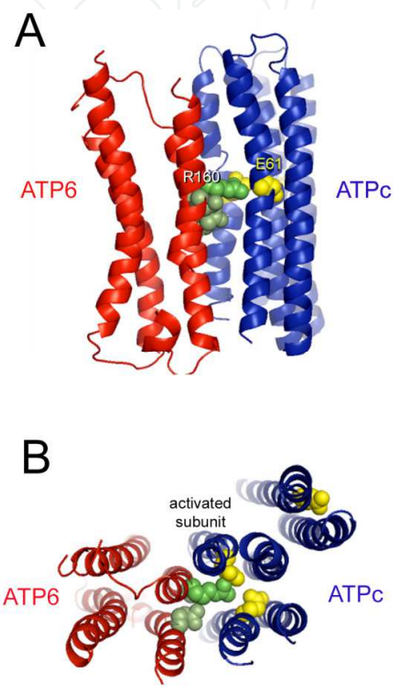
In the fruit fly *Drosophila melanogaster* and the California purple sea urchin *Strongylocentrotus purpuratus* the gene expression of the ATP-synthase subunit alpha (*atpα*) was measured at early developmental stages, and it was found that the amount of mRNA varies throughout development in both species. Contrary results showed that during the larval stage the nuclear and mitochondrially encoded ATP synthase genes appear to be temporally co-regulated in *Drosophila*, although in the sea urchin this development pattern was not observed (Talamillo et al., 1998). In 2005, Kidd et al. analysed null mutants of the *A*TP-synthase subunit ε in *Drosophila* spp., and a dramatic delay in the growth rate of the first instar larvae that finally died was reported. In addition, in fly embryos the ATP-synthase activity had a six-fold reduction.

Most likely, the first two studies concerning the ATP synthase of crustacean species were published in 2001. The authors characterised the enzymatic properties of F_1 and evaluated its sensitivity to specific inhibitors and modulators in the gills of the freshwater crayfish *Orconectes virilis*; they included, as an important contribution, the standardised methods for isolating mitochondria from crustacean tissues and some results about their enzyme stability at different temperatures and pH conditions (Li & Neufeld, 2001a, 2001b).

Recent reports on the most-studied shrimp species – *Litopenaeus vannamei* – have characterised and studied several mitochondrial and nuclear encoded subunits from tissues such as muscles, gills, pleopods and the midgut gland (Muhlia-Almazan et al., 2008; Martinez-Cruz et al., 2011). The complementary DNA sequences of the *atp6* subunit encoded in the mtDNA and the *atp9* (a nuclear encoded subunit) were characterised and their deduced proteins, as major components of the F_O sector, were included in a molecular model which predicted that in the shrimp F_OF_1 ATP synthase the *atp9* oligomeric ring may contain 9-10 proteins (Figure 1; Muhlia-Almazan et al., 2008).

Over the last decade, the effects of a viral agent which provokes shrimp death have been deeply studied. The white spot syndrome virus (WSSV) is perhaps the most devastating shrimp disease, causing massive mortalities in global aquaculture systems (Sanchez-Paz, 2010). In 2006, Wang et al. analysed the gene expression profile of the fleshy prawn *Fenneropenaeus chinensis* in response to WSSV infection through cDNA microarrays. Genes including the ATP-synthase A chain and arginine kinase were found to be down-regulated during WSSV infection. Additional studies in other shrimp species, reported thirty additional genes which are involved in the antiviral process as part of the shrimp's defence system. One of the most interesting findings of these studies was that the interferon-like

protein (IntlP) – known as an antiviral factor – showed increased expression in virus-resistant shrimp (He et al., 2005). Later, Rosa & Barraco (2008) suggested that the shrimp interferon-like protein (IntlP) is rather a region of the insect mitochondrial b subunit of the ATP-synthase, due to the high identity between both proteins (60–73%). Recently, Liang et al. (2010) have suggested the ATP-synthase subunit β (*atp* β) - earlier called BP53 – as a protein involved in the WSSV binding to shrimp cells that may play an important role in the antiviral defence system of shrimp against WSSV.



A) Ribbon lateral view, and B) Ribbon front view of the subunit ATP6 complex with three ATP9 subunits. The predicted functional residues are marked in both subunits, R160 from ATP6, and E99 from ATP9. (Taken from Muhlia-Almazan et al., 2008).

Fig. 1. Molecular Model of the ATP9- ATP6 Subcomplex from the Shrimp *L. vannamei*.

Transcriptomes and proteomes have provided a lot of information, not only about the characteristics of specific sequences of nucleotides or amino acids, but also about the proteins' structure and function in invertebrate organisms under diverse environmental conditions (Clavero-Salas et al., 2007). Moreover, novel proteins have been reported as accessories to the mitochondrial protein complexes in invertebrates species, such as the ticks *Ornithodoros moubata* and *O. erraticus*, where six novel proteins similar to the ATP synthase subunit 6 (*atp6*) were identified in the salivary glands. These proteins are attractive targets for controlling ticks and tick-borne pathogens (Oleaga et al., 2007).

Actually, and based in the mitochondrial highly conserved function, generic models of the electron transport chain in mitochondria have been constructed using bioinformatic tools to predict how the rate of oxygen consumption through the system – and the redox states of some intermediates such as NAD/NADH, ubiquinone, and cytochromes – respond to physiological stimuli such varying oxygen levels and other rapid energy demands (Banaji, 2006).

Ultimately, it is remarkable that the mitochondrial function has remained in all animal species through its long and peculiar evolutionary history and under the influence of variable selective pressures. Moreover, structural and biochemical adaptations promoting highly effective mitochondrial functions have allowed organisms to inhabit unusual environments.

3. The Invertebrates mitochondrial genome

The study of the mitochondrial genome has provided enormous amounts of information from which it has become feasible to infer the origin of species by using comparative and evolutionary genomics (Jiang et al., 2009) in order to understand the ancient phylogenetic relationships among species, to comprehend population genetics (Boore et al., 1995; Boore, 1999), and to recognise the mechanisms coordinating the nuclear and mitochondrial genomes so as to synthesise a large number of functional proteins located in this organelle.
To date, the mtDNA of several invertebrates has been sequenced and characterised, including ascidians (Yokobori et al., 1999), echinoderms (Jacobs et al., 1988; Asakawa et al., 1995), insects (Clary & Wolstenholme, 1985), nematodes (Okimoto et al., 1992), molluscs (Yu & Li, 2011; Cheng et al., 2011), and various crustacean species such as shrimp and crabs (Staton et al., 1997; Shen et al., 2007; Peregrino-Uriarte et al., 2009). Several reports have shown that the mitochondrial genome of invertebrate species varies, and ranges between 12 and 20 kbp. This may be due to contrasting ecological habitats or it may be a response to different selective pressures (Table 1).

Phylum	Species	mtDNA size (bp)	GenBank Acc. No.	References
Porifera	*Plakinastrella sp.*	19,790	NC_010217	Lavrov et al., 2008
	Negombata magnifica	20,088	NC_010171	Belinky et al., 2008
	Aphrocallistes vastus	17,427	NC_010769	Rosengarten et al., 2008
Cnidaria	*Hydra oligactis*	16,314	NC_010214	Kayal & Lavrov, 2008
	Aurelia aurita	16,937	NC_008446	Shao et al., 2006
	Fungiacyathus stephanus	19,381	NC_015640	---
Platyhelminthes	*Symsagittifera roscoffensis*	14,803	NC_014578	Mwinyi et al., 2010
	Clonorchis sinensis	13,877	JF729304	Cai et al., 2011
	Taenia taeniaeformis	13,647	NC_014768	Liu et al., 2011
Rotifera	*Brachionus plicatilis*	12,672	NC_010484	Suga et al., 2008
Acanthocephala	*Leptorhynchoides thecatus*	13,888	NC_006892	Steinauer et al., 2005

Phylum	Species	mtDNA size (bp)	GenBank Acc. No.	References
Nematoda	*Caenorhabditis elegans*	13,794	NC_001328	Wolstenholme et al., 1994
	Necator americanus	13,605	AJ417719	Hu et al., 2002
Onychophora	*Oroperipatus sp.*	14,493	NC_015890	Segovia et al., 2011
Brachiopoda	*Laqueus rubellus*	14,017	AB035869	Noguchi et al., 2000
Echinodermata	*Acanthaster planci*	16,234	NC_007788	Yasuda et al., 2006
	Strongylocentrotus purpuratus	15,650	NC_001453	Qureshi & Jacobs, 1993
	Cucumaria miniata	17,538	NC_005929	Arndt & Smith, 1998
Mollusca	*Crassostrea gigas*	18,225	EU672831	Ren et al., 2010
	Cepaea nemoralis	14,100	NC_001816	Terrett et al., 1996
	Octopus minor	15,974	HQ638215	Cheng et al., 2011
Annelida	*Platynereis dumerilii*	15,619	AF178678	Boore & Brown, 2000
	Lumbricus terrestris	14,998	NC_001673	Boore & Brown, 1995
Arthropoda				
Subphylum Chelicerata	*Centruroides limpidus*	14,519	NC_006896	Davila et al., 2005
Subphylum Crustacea	*Litopenaeus vannamei*	15,989	DQ534543	Shen et al., 2007
Subphylum Myriapoda	*Scutigera coleoptrata*	14,922	NC_005870	Negrisolo et al., 2004
Subphylum Hexapoda	*Apis mellifera*	16,343	NC_001566	Crozier & Crozier, 1993

Table 1. Invertebrates' mitochondrial genome size of the species of different phyla.

Because of the wide variability of environmental conditions in which a large number of invertebrate species are distributed, several specific mtDNA-rearrangements have been found when compared with those observed in the mtDNA of mammals. Such novel arrangements include the mitogenome from the blue mussel *Mytilus edulis* (Hoffmann et al., 1992), and that of the fruit fly *Drosophila melanogaster* (Clary & Wolstenholme, 1985; Garesse, 1988) and the horseshoe crab *Limulus polyphemus* (Staton et al., 1997).

Also, some species – or groups of species – may lack some genes, such as nematodes whose mtDNA lacks a gene for ATP8 (Keddie et al., 1998), or cnidarians like the coral *Sarcophyton glaucum* which includes an unusual gene encoding an extra tRNA (Beaton et al., 1998). Moreover, major changes have been found in invertebrates' mtDNA, such as the mitochondrial genes of *Lumbricus terrestris*, which are all known to be encoded in the same strand and, unlike others, the genes coding A8 and A6 are separated by a long 2700 nucleotides fragment (Boore & Brown, 1995).

In 2006, the description of the mtDNA of the moon jellyfish (*Aurelia aurita*) was reported. It was surprising to find that mitochondria of this organism contain a linear genome, which became the first non-circular genome described in a Metazoan. Besides its linearity, its organisation involves two additional sequences of 324 and 969 nucleotides, the last (ORF969) encodes a putative family B-DNA polymerase, tentatively identified as *dnab,* which was previously only reported in algae mtDNAs (Shao et al., 2006). Subsequently, the linear mitogenome of Cnidarians of the genus *Hydra* was also reported, although it was found that it is fragmented as two linear mitochondrial "chromosomes" (mt1 and mt2) where all genes are unidirectionally-oriented (Voigt et al., 2008).

In addition, the invertebrate's mitochondrial genetic code differs from the universal/standard genetic code, and it is suggested that this is species-specific since several studies have identified some changes in animal mitochondrial code, as shown by Table 2 (taken from Watanabe, 2010). As observed in this table, invertebrate mtDNAs are largely represented by different changeable codons – depending upon the species. This is the case for the AUA codon which usually codes Ile in the standard genetic code but in the mitochondria of some species of Nematoda, Mollusca, Platyhelminthes and Vertebrata it encodes a Met (Himeno et al., 1987; Bessho et al., 1992). Also, in several species, the start codon differs from the AUG but still codifies a methionine, and in most of the species the stop codon is an incomplete codon, such as UA or U (Watanabe, 2010).

Codon (Universal code)	**AUA (Ile)**	**AAA (Lys)**	**AGA (Arg)**	**AGG (Arg)**
Vertebrates (human, bovine, rat, mouse, chicken, frog)	**Met**	Lys	**Term**	**Term**
Prochordates (ascidian, asymmetron)	**Met**	Lys	**Gly**	**Gly**
Echinoderms (sea urchin, starfish)	Ile	**Asn**	**Ser**	**Ser**
Arthropods	**Met**	Lys	**Ser**	**Ser**
Most (shrimp, daphnia)	**Met**	Lys	**Ser**	**Ser**
Insect (Drosophila)	**Met**	Lys	**Ser**	-
Molluscs (squid, octopus, Liolophura, Mesogastropoda)	**Met**	Lys	**Ser**	**Ser**
Nematodes (nematodes, ascaris)	**Met**	Lys	**Ser**	**Ser**
Platyhelminthes	**Met**	**Asn**	**Ser**	**Ser**
Most (Echinostomida, Trematoda)	Ile	**Asn**	**Ser**	**Ser**
Rhabditophora (Planaria)	Ile	Lys	Arg	Arg
Coelenterates (jellyfish, coral, sea anemone, hydrozoa)	Ile	Lys	Arg	Arg

Table 2. The relationships between the genetic codes of animal mitochondria. Modified from: Watanabe, 2010. Bold letter: non-universal codon; Term: termination codon.

Although, to date, the mitochondrial genes expression mechanisms are not fully understood, and the evolutionary processes by which the mitogenome suffers a rearrangement are not clear. It is proposed that a new order in genes' arrangements must preserve or facilitate those signals or mechanisms required for the transcription and processing of RNAs to accomplish the mitochondrial function in animal species (Boore, 1999).

The mitochondrial DNA from animal cells is known to be easily affected, since it is not protected by DNA-binding proteins or histones such as nuclear DNA. Several studies have found that mtDNA can be affected by aging, hypoxia and random events of mutation or insertion/deletion (rates of mutation for mitochondrial genomes are known to be much higher than those in the nuclear DNA) that can produce increased oxidative stress and high levels of ROS in this organelle. Defective proteins which result from altered mtDNA molecules cause defective mitochondrial function, as an impaired respiratory chain and increased electron leaks so as to finally generate larger amounts of ROS (Wei et al., 1998).

Insects' mitogenomes are known to be affected at the transcriptional level by chemicals, since the mtDNA copy number has been shown to increase to meet the bioenergetic demands of the organism, as observed in the fly *D. melanogaster* when exposed to tetracycline. Treatment with this antibiotic causes an energetic deficiency, promoting an up-regulation of the mtDNA copy number (Moraes, 2001; Ballard & Melvin, 2007).

4. Invertebrate challenges and how marine species spend energy

In most animal species, high energy levels in their bodies reveal fast growth, adequate energy storage, effective reproduction strategies and viable descendants with characteristic short life spans; however, reduced energy levels in a biological system results in affected gene expression, low survival rates and reduced metabolic rates and, therefore, a need on the part of physiological mechanisms to slow the ageing rate until environmental conditions are enhanced and higher energy levels are again reached (Stuart & Brown, 2006). In their natural habitat, many invertebrate species must undergo endogenous physiological processes during their life cycle, such as molting, starvation, quiescence and metamorphosis, among others. Many of these processes imply high energetic expense, causing a low energy status that reduces their ability to reach the adult stage (Hochachka & Somero, 2002).

The role of metamorphosis – one of the most amazing physiological endogenous processes in nature – becomes strikingly important when considering the large number of animal species that undergo metamorphic changes. Frequently, the energetic balance of holometabolous insects during metamorphosis is negative, because there is no energy gain and species must face all these changes by using any energetic reserves previously stored (Nestel et al., 2003).

During their larval stages, insects – such as Lepidopterans – show fast growth rates, as observed in the tobacco worm larvae of *Manduca sexta* which increases its mass 10,000-fold in just 16 days at the final larval instar (Goodman et al., 1985). The midgut epithelium of this species is a highly aerobic tissue that digests and absorbs nutrients, and transports ions at high rates. During metamorphic changes, the midgut epithelium is programmed to die and the larval midgut should maintain structural and functional integrity until the pupal epithelium is formed. During this process, ATP synthesis and mitochondrial function must be obligatorily maintained. Thus, organisms resolve this by reducing mitochondrial

substrate oxidation, a clear indication that the electron transport chain may be a site of modulation during metamorphosis (Chamberlin, 2004).

Quiescence and estivation are also two responses that some species may display during unfavourable environmental conditions in which insufficient energy is available to grow and breed. These dormant states allow species to survive by reversibly down-regulating their metabolism to low levels for up to several years. Among invertebrates, many species show quiescent states at stress conditions, including nematodes, crustaceans such as the brine shrimp *Artemia franciscana* (Hand, 1998), the estivating pulmonate snail *Helix aspersa* (Pedler et al., 1996), and various insect species entering in diapause, such as *Helicoverpa armigera.* Studies have proposed that a coordination mechanism is required when animals enter into the dormant state so as to maintain cellular homeostasis by both energy-consuming and energy-producing pathways. During quiescence, *A. franciscana* can reduce its metabolism essentially to zero, this metabolic-rate suppression affects the mitochondrial respiratory capacity and the rates of ATP-consuming processes (Barger et al., 2003). In the embryos of *Artemia franciscana*, anoxia provokes the organism to enter into a quiescent state. During experimental gradual oxygen removal, various biochemical responses are observed, such as a pH decrease, the reduction of heat production and the depression of ATP levels. Also, genetic responses, such as the down-regulation of RNA transcription, are observed during quiescence (Hand, 1998).

Often, metabolic rates have been inversely related to the life span of mammals. Moreover, when mitochondrial respiration has been inhibited by RNAi techniques, the life span extends in *C. elegans* (Lee et al., 2003), and long-lived mutants of this nematode concomitantly show decreased metabolic rates (Stuart & Brown, 2006).

The process by which mitochondrial respiration affects or extends life span has been studied in several organisms, including yeasts, worms, flies and mice (Lee et al., 2010). Electron transport in mitochondria is the main producer of superoxide anion ($O^{\cdot-}$), which in turn generates several types of reactive oxygen species (ROS), as has been mentioned (mitochondrial Complex III). In fact, according to various studies, ROS are not only undesirable toxic metabolites promoting organism oxidative stress, but they are also molecules that participate in the mitochondria-nucleus's signalling pathways (Storz, 2006). Emerging data on *C. elegans* suggests a new described pathway where superoxide serves as an intracellular messenger, whereby with increasing superoxide concentration a signal transduction pathway is triggered, resulting in changes in the pattern of gene expression of nuclear proteins and which finally results in an increased life span (Yang & Hekimi, 2010). However, different mechanisms have also been proposed as being implicated in the aging process, such as diet restriction, ubiquinone deficiency and the hypoxic response (Klimova & Chandel, 2008).

At this point, this chapter would not be complete if the energetic costs of flying for insect species were to be omitted. This activity is probably the most expensive process recorded in nature. It is by now a well-known and remarked-upon fact that the metabolic rate during insect flight increases over 50-100 fold above the resting rate (Ellington, 1985). Thus, it is clear that the flight muscle of insects is the model tissue that many researchers have adopted in order to understand mitochondrial function since it is capable of effectively producing and hydrolysing large amounts of ATP (Sherwood et al., 2005). Insect flight is a highly oxygen-dependent process, and the flight muscle metabolism is fully aerobic; thus, it has

been suggested that the amazing aerobic capabilities of insects are based on a highly efficient mode of oxygen delivery that includes their oxygen transport system in a well distributed system of tracheae and tracheoles (Wegener, 1996).

In addition, several studies have demonstrated that the function and energy needs of certain tissues are highly correlated with the number of mitochondria per cell (Robin & Wong, 1988). This agrees with the large quantities of mitochondria with pronounced cristae and large surface areas that are found in the flight muscle cells of the honey bee *Apis mellifera* (Suarez et al., 2000). To date, it is well-known that oxygen uptake rates in mitochondria cristae are much higher in the flying muscle of *A. mellifera* than that observed in mammals' mitochondria – this can explain the higher electron transport rates observed in such enzymes as cytochrome c oxidase, whose maximum catalytic capacity was recorded in this species during flight - (Suarez et al., 2000).

Besides the increase on the ATP hydrolysis rate during flight, other mitochondrial adaptations to the highly and continuous energy requirements of flying species have been reported, such as the remarkable dependence on the synthesis of energy-rich phosphate compounds like phosphoarginine. Phosphoarginine, as mentioned above, constitutes a usable pool of high energy phosphate (Hird, 1986) so as to maintain the high rate of ATP turnover in flying insects (Wegener, 1996).

In addition to the various metamorphic changes in their life, crustaceans undergo a frequent and cyclic process: molting. During the molt cycle, crustaceans are exposed to a temporary scarcity of food since they lack the ability to handle food until their new exoskeleton is synthesised. Several adaptive strategies have been recognised as being employed by these organisms so as to avoid the adverse effects of starvation, such as the storage of fuel compounds in their midgut gland (Sanchez-Paz et al., 2007), changes in locomotor activity (Hervant & Renault 2002), and a decrease in oxygen consumption (Morris et al., 2005). However, little attention has been paid to the bioenergetic consequences of starvation in shrimp; since the composition of food plays an important role in oxidative phosphorylation, the nutritional status of shrimp species, such as *Litopenaeus vannamei*, may affect its major bioenergetic functions.

In our lab, we have hypothesised that, due of its central role in the cell energy metabolism, the expression of genes encoding the different polypeptide subunits that compose ATP synthase during unpredictable episodes of food shortage may ultimately be modulated. Thus, we experimentally evaluate the effect of starvation in the gene expression of subunits *atpα, atpβ* and *atp*in the shrimp midgut gland, during a period of short-term food deprivation (5 days). Our results (Figure 2) show that the mRNA amounts from subunits *atpα* and *atpβ* which directly participate during ATP synthesis decreased as starvation time increased; however, no significant changes were observed in the mRNA amounts of *atp9*, which forms the oligomeric ring from Fo in the shrimp ATP-synthase.

Sanchez-Paz et al., (2007) reported a gradual decrease of glycogen in the midgut gland of the white shrimp as starvation progressed. After a 24 h starvation period, the glycogen content dropped by about 50%, which correlates with an increase of the *atp*9 subunit after 24 h of starvation, suggesting that glycogen may be used as fuel to generate ATP and pyruvic acid. As glycogen stores become depleted, the organism must increasingly rely on fatty acid catabolism as a source for ATP synthesis. In general, starved shrimp showed a sharp decrease in their midgut gland lipidic constituents for up to 120 h (more noticeable in acylglycerides).

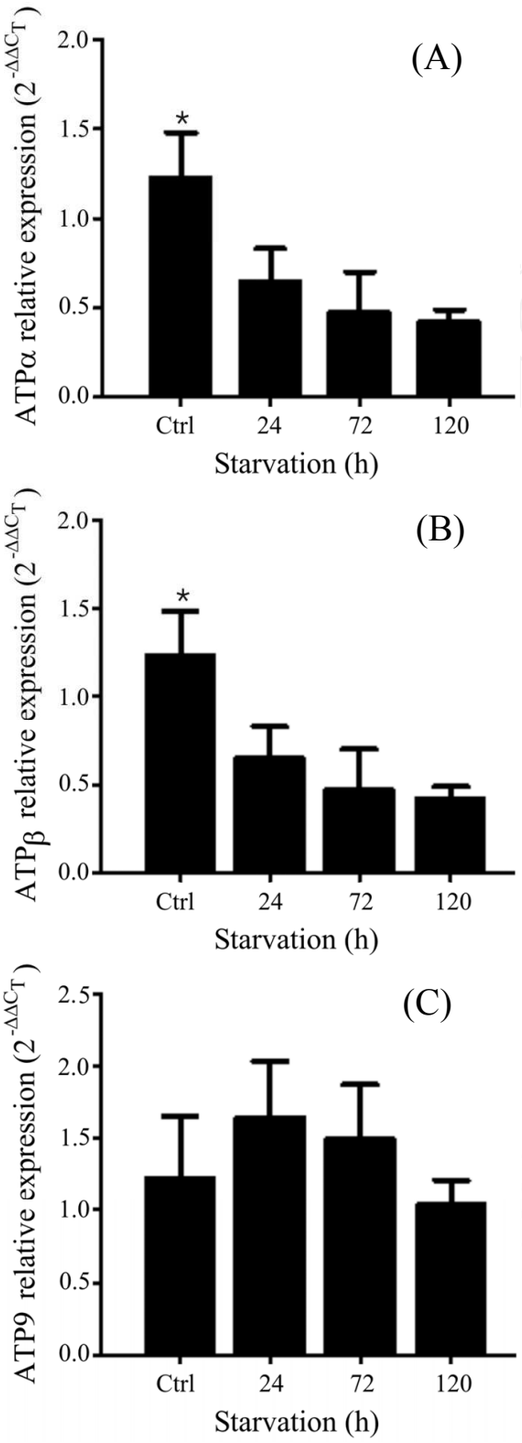


Fig. 2. The relative expression of A) ATPα, B) ATPβ and C) ATP9 mRNA in the midgut gland of the white shrimp *Litopenaeus vannamei* in response to a short-term starvation period. Expression values are given based on normalisation to L8. The data is represented as the mean and standard deviation of triplicate determinations. (*) Statistical significance was considered at $P < 0.05$.

Various studies have shown that during starvation-induced lipolysis there is a decrease in the amount of ATP, which was accompanied by a fall in some subunits of the FoF_1-ATP synthase (Vendemiale et al., 2001). It is well-known that starvation tampers with cellular detoxification systems and may expose cells to oxidative injury (Di Simplicio et al., 1997; Vendemiale et al., 2001), leading to an impaired production of ATP and a reduced uptake of substrates for mitochondrial metabolism. The results from our study, together with results from previous studies, prompt us to suggest that shrimp are capable to satisfy their energy demands through a complex combination of mechanisms that enables them to survive the adverse effects of food scarcity.

Due to its density, viscosity (800 times more dense and 50 times more viscous than air) and low oxygen solubility, water – as a respiratory medium – imposes difficulties for aquatic breathers in obtaining the necessary supply of oxygen from their surrounding environment so as to keep breathing and bringing oxygen into their systems. This process becomes more complicated when considering additional parameters (such as temperature, salinity and depth) affecting the dissolved oxygen concentration of seawater, causing additional constraints on marine species' development (Sherwood et al., 2005). All the species inhabiting marine environments should face these dynamic environmental conditions, which in over the last few decades have been seriously affected by a wide variety of anthropogenic activities, such as industrial and agricultural runoffs (Wu, 2002).

Several studies have found that marine invertebrates may respond to stress conditions by changes at the transcriptional level. In crustacean species such as the crab *Eriocheir sinensis*, different gene expression profiles from gills were characterised during acclimation to high cadmium concentrations in water. Analyses have revealed over-expressed genes, such as disulphide isomerase, thioredoxin peroxidase and glutathione S-transferase. Under the same conditions, ATP synthase beta, alpha tubulin, arginine kinase, glyceraldehyde-3-phosphate dehydrogenase and malate dehydrogenase were down-regulated. The results demonstrated that acute and chronic exposure to waterborne cadmium induced a decreased abundance of the transcript-encoding enzymes involved in energy transfer; this suggests that chronic metal exposure induced an important metabolic reorganisation (Silvestre et al., 2006).

Some other species which face high cadmium concentrations are marine intertidal molluscs, such as oysters, which live in estuaries were fluctuating temperatures and levels of trace metals are known to directly affect mitochondrial function. Isolated mitochondria from the oyster *Crassostrea virginica* which were exposed to low cadmium concentrations (1 $\mu mol \cdot L^{-1}$) resulted in a progressive uncoupling that increased with the increasing dose of cadmium; this response agrees with that observed in mammals. However, unlike mammals, molluscs are ectotherms and the exposure to the combined effects of high temperatures and cadmium concentrations severely affected mitochondrial function since elevated temperatures increased the sensitivity of this organelle to cadmium and promoted an increase in the rate of ROS production (Sokolova, 2004). These results highlight the key role of temperature in the mitochondrial system of ectotherm species.

Most invertebrates are described as ectotherm species because their body temperatures vary with the environment. At very low temperatures, polar marine invertebrates were expected to show low metabolic rates, as previously observed in Antarctic fish; however, in 1999 Sommer & Portner found important intraespecific differences in the mitochondrial function of the polychaete *Arenicola marina* from the North Sea and the colder White Sea. Their results

concluded that invertebrate life is more costly at higher latitudes, where oxygen uptake, tissues mitochondrial densities and mitochondrial capacities were higher.
Remarkable abilities have been recorded in invertebrate species inhabiting extreme environments. The term "metabolic plasticity" perfectly describes such organisms as the intertidal periwinkle snail *Littorina littorea*, which has the ability to deal with very low temperatures and also to tolerate the changing environmental conditions imposed by the tidal cycle, implying continuous oxygen deprivation (Storey, 1993). Besides the biochemical and physiological mechanisms previously identified in this species, the over-expressed gene encoding a metallothionein (MT) was recently found during the exposure to low temperature and anoxic conditions of the tissues of *L. littorea*. Since thermogenesis is a process that requires high oxygen consumption and since it is also accompanied by a sharp rise in reactive oxygen species (ROS) generation, the authors describe the ability of MT to function as an antioxidant and as a reservoir of essential metals that contributes to survival under these conditions (English & Storey, 2003).
The deep sea hydrothermal vents are a different type of extreme environment where thermophilic species such as the Pompeii worm *Alvinella pompejana* inhabit. Shin et al. (2009) studied the structure and biochemical characteristics of the Cu,Zn-superoxide dismutase (SOD) of this species and found striking similarities between this enzyme and that of humans, but with an enhanced stability and catalysis – characteristics that may mean that this enzyme is potentially suitable for scientific and medical application. Other mitochondrial proteins have been proposed as a part of gene therapy for devastating human diseases by preventing the cell damage caused by oxidative stress. AOX – the mitochondrial alternative oxidase previously mentioned – is suggested to work in any cell, becoming chemically active only when it is required. AOX is provided to the cell by engineering a gene from a marine invertebrate snail *Ciona intestinalis*; this protein is under analysis as a therapeutic tool tested in mammalian disease models (Hakkaart et al., 2006).

5. How do invertebrates face hypoxia?

Hypoxia is probably one of the most studied factors affecting the central metabolic pathways of living organisms, including invertebrates. Aquatic species usually face hypoxic events in freshwater or marine environments as a daily cyclic routine in the shallow waters of lagoons, estuaries and mangroves during the dark hours, when plants and algae do not produce oxygen and organic matter is continuously oxidised (Dall et al., 1990). However, nowadays the frequency, abundance and severity of hypoxic events in coastal waters have increased due to anthropogenic activities resulting in deteriorating environments affecting marine organisms (Diaz, 2001). It is well known that hypoxia depresses the growth rate of marine animals, as it disturbs metabolic pathways and promotes the reallocation of energy resources (Wei et al., 2008; Wang et al., 2009).
Several studies have examined the physiological responses of invertebrate species to hypoxia, such as growth, stress resistance and even behaviour patterns in aquatic species able to vertically and horizontally migrate through the water column to reach more oxygenated zones (Eads & Hand, 2003; Burgents et al., 2005; Abe et al., 2007; Seibel, 2011). In fact, among invertebrates there are hypoxia-tolerant species, such as bivalve molluscs and annelids, with highly adapted structures and mechanisms to deal with hypoxia, and some others, such as crustaceans, whose tolerance to hypoxia depends on their habitat, food, and energy needs. Unfortunately, the responses to hypoxic conditions – at the molecular and

biochemical levels – of the mitochondrial proteins and enzymes that participate in the respiration process are still poorly studied for most invertebrate species.

The main physiological responses from invertebrates to hypoxia are somewhat similar to those from vertebrates since in the reduction or absence of oxygen, animal cells are not able to produce enough energy to survive. Such general responses are clearly a legacy of the evolutionary past from ancestral forms and they serve adaptive ends. In marine species, such as crustaceans and molluscs, reduced oxygen consumption and metabolic rates have been confirmed during hypoxia; in addition, glucose utilisation and lactate accumulation as indicators of a switch to anaerobic metabolism have been detected at low oxygen concentrations in water (Racotta et al., 2002; Martinez-Cruz, 2007; Soldatov et al., 2010). In the brine shrimp *A. Franciscana*, the intracellular pH falls at anoxia, heat production is reduced and ATP concentrations are also depressed to low levels (Hand, 1998; Eads & Hand, 2003).

A large amount of information is now available about the changes at the transcriptional level promoted by hypoxia in invertebrates, most of it concerning aquatic species. In our lab, we have evaluated the effects of hypoxia in the gene expression of F_OF_1 ATP synthase subunits, such as *atp9, atp6, atpα, atpβ, atpγ, atpδ, and atpε*, in different tissues of the white shrimp *L. vannamei*. Results show a general trend towards increase the amount of mRNA as oxygen concentrations decrease (Martinez-Cruz, 2007; Martinez-Cruz et al., 2011; Martinez-Cruz et al. in preparation). Also, significant changes in the amount of mRNA from the mitochondrial- and nuclear- encoded subunits of the ATP synthase were detected at different molt stages and tissues, according to the energy requirements of each stage and the specific requirements of the function of each tissue (Muhlia-Almazan et al., 2008). Chronic exposure to severe hypoxia (1.5 mg/mL during 7 days) also causes the increased transcription of mitochondrial-encoded genes, such as the 16S, CO1, and CO2 subunits from the cytochrome C oxidase in the grass shrimp *Palaemonetes pugio* (Brouwer et al., 2008). To date, microarray technologies have revealed a set of genes that are up- and down-regulated in *P. pugio* during chronic, acute and moderate hypoxia; the results revealed that various genes encoding mitochondrial proteins were affected (Li & Brouwer, 2009).

In the absence of oxygen, animal cells activate transcription factors – such as the well-studied vertebrates hypoxia-inducible factor (HIF) – which has been reported in invertebrates from worms to flies (Semenza, 2007). When activated, HIF leads the organism to exhibit metabolic adaptation to hypoxia by regulating the genetic expression of some proteins and enzymes involved in central biological processes such as glycolysis, erythropoiesis, breathing and angiogenesis so as to maintain cell homeostasis (Klimova & Chandel, 2008). In the shrimp *P. pugio*, a homolog protein to HIF-α called gsHIF was found in this hypoxia-tolerant species. It includes all the conserved domains of vertebrates' HIF proteins, and an additional polypeptide sequence of 130 residues that has not been found in databases, and its participation in the functional properties of the protein has not yet been determined (Li & Brouwer, 2009). In the white shrimp *L. vannamei*, HIF-1 is a heterodimer formed by two subunits: HIF-1β, which is constitutively expressed in shrimp cells and HIF-1α, which is differentially expressed in hypoxic conditions. HIF-1 is suggested in crustaceans to be the master regulator that senses decreased oxygen availability and transmits signals promoting the physiological responses mentioned above (Soñanez-Organis et al., 2009). Additional functions have been attributed to HIF in coral species, such as *Acropora millepora*, where the diel cycle in the central metabolism appear to be governed by the circadian clock and regulated by the HIF system operating in parallel (Levy et al., 2011).

As a part of the HIF-regulated metabolic responses to hypoxia in invertebrates, the activities of specific enzymes – most of them part of the central metabolism – are known to increase. In bivalves such as *Anadara inaequivalvis*, the increased activities of enzymes – such as malate and lactate dehydrogenases – were detected at hypoxia (Soldatov et al., 2010). Also, increases in the catalase and GST activities during anoxia in the estuarine crab *Chasmagnathus granulate* have been observed. It has been suggested that such responses may be a strategy to prepare the organisms for oxidative stress in an effort to protect tissues against oxidative damage during re-oxygenation. An important decrease in SOD activity (which occurred after aerobic recuperation) was also detected; and it could have been caused by the accumulation of hydrogen peroxide production during re-oxygenation (de Oliveira et al., 2005).

At normoxia, the small levels of ROS produced by the metabolism in normal animal mitochondria come from carrying electrons along the mitochondrial complexes I, II, and III (Turrens, 2003). However, when oxygen levels are reduced, the presence of the final electron acceptor in the mitochondrial respiratory chain fails, producing a reduction in the rate of electron transport and a decrease in oxygen consumption. Under these conditions, the membrane potential increases as does ROS production (Guerrero-Castillo et al., 2011).

It has been reported that in invertebrate species considered to be hypoxia-tolerant, the absolute rate of H_2O_2 production is at least an order of magnitude less per mg of mitochondrial protein than that measured on mammalian species (Abele & Puntarulo, 2004). However, some other species which are not tolerant to hypoxia tend to produce higher levels of ROS at low oxygen levels; thus, it is suggested that they display alternate pathways in order to maintain the mitochondrial respiratory rate and avoid an over-production of ROS (Guerrero-Castillo et al., 2011).

Nowadays, the alternative mechanism of proton sinks has been evidenced in invertebrates since uncoupling proteins (UCPs) have been identified in these species (Abele et al., 2007). Such proteins have been involved in various functions, including thermoregulation, body composition, antioxidant defence and apoptosis. UCPs are thought to dissipate the proton gradient across the inner mitochondrial membrane and may help in controlling ROS production (Yu et al., 2000).

In *Drosophila*, an UCP5 protein over-expressed in a heterologous system has shown to have similar functional abilities to an uncoupling protein (Fridell et al., 2004), while in the marine eastern oyster, *Crassostrea virginica*, UCP5 is represented by two transcript forms: UCP5S (small) and UCP5L (large). However, their function has not been determined since its gene expression is not affected by hypoxia, cadmium exposure or different temperatures (Kern et al., 2009). In addition, a novel protein (UCP6) in invertebrates is considered to be an ancestral form of the vertebrates UCP1, UCP2, and UCP3 (Sokolova & Sokolov, 2005).

In mammals, it is known that less-severe hypoxia induces protective mechanisms. This phenomenon – called hypoxic preconditioning (HP) – appears in two forms: immediate preconditioning (which occurs only a few minutes after a sub-lethal hypoxic episode and declines after 4 h) and delayed preconditioning (which requires gene expression changes and takes place 12 to 24 h later and can last for days) (Dirnagl et al., 2009). In the nematode *C. elegans*, the delayed form of HP has been found to induce unfolded protein response pathways – at this point, misfolded proteins serve as early hypoxic sensors that trigger signalling pathways to induce a hypoxia protective response (Mao & Crowder, 2010).

6. The role of mitochondria in invertebrate programmed cell death (Apoptosis)

Besides the various functions just described, mitochondria also acts as the arsenal of the cell. Numerous and complex processes, still poorly understood, can trigger the release of mitochondrial components into the cytoplasm and subsequently induce cellular apoptosis of the organelle (Hengarter, 2000). It is not our intent here to provide exhaustive coverage of all the issues relating to apoptosis in great detail, but rather to give the reader a basic description of the process – to highlight its importance and to show the challenges that those interested in this topic will face.

As has been mentioned, studies in invertebrate biology are paramount to an understanding of biodiversity and to the search for potential uses for their metabolic capabilities and products for biotechnologies. Besides, comparative sciences may facilitate the use of invertebrate models in understanding the biology and pathology of farmed animals and humans. This is due – in spite of differences in the biochemical, physiological, and cellular characteristics that make invertebrates and vertebrates so obviously different – to the fact that most parts of such grades of their biology have remained similar in both groups through their evolution. For example, invertebrate cells – whether wounded by harsh environments or by the expression of abnormal proteins – die as do vertebrate cells, indicating that the powerful advantages of invertebrate molecular genetics might be successfully used for testing specific hypotheses about human diseases, for the discovery of drugs and for non-biased screens for suppressors and enhancers of maladies (Driscoll & Gerstbrein, 2003). The same criteria apply for all cellular functioning, as for apoptosis.

Apoptosis (from the Greek: "falling off") – or programmed and regulated cell death and elimination – is a pivotal process in embryogenesis, the orderly elimination of wounded or infected cells, and the maintenance of tissue homeostasis. The process is so important that it is estimated that on a daily basis the human body must get rid of approximately 10^{10} cells. Through apoptosis, cells die quietly in a controlled, regulated fashion; while in another forms of cell death – such as in necrosis – a series of uncontrolled events occur leading to serious and irreversible damage. Given the proper conditions, apoptosis destroys the cell swiftly and neatly. In contrast, necrosis causes the rupture of the cell, releasing its content into the surrounding tissue. Tampering with apoptosis may result in devastating health problems, such as cancers, immune diseases, neurodegenerative disorders and the proliferation of viruses. Apoptosis is executed by a variety of membrane, organelle, cytoplasmic and nucleus signalling, and initiator and effector molecules, including a subfamily of cysteine proteases known as caspases (Jiang & Wang, 2004).

In mammals, the active role of mitochondria in apoptosis induction has been well-established. In invertebrate models of apoptosis, such as the fly *Drosophila melanogaster* and the worm *C. elegans*, the role that mitochondria play during apoptosis and, in particular, during apoptosis initiation is less clear (Rolland & Conradt, 2006). While key regulators of apoptosis in *Drosophila* and *C. elegans* have been found in association with mitochondria, the significance of these associations has not been rigorously tested.

The regulated destruction of a cell is a basic process in Metazoa, as multicellular animals are obligated to remove damaged or harmful cells. During apoptosis, cells die in an orderly, regulated sequence of molecular, biochemical, and cellular processes. According to the endosymbiotic theory, the origin of apoptosis is currently regarded as the result of molecular interactions in which some components of a signal transduction pathway affects

other pathways through interaction of some initiator and effector proteins. Accordingly, apoptosis could have arisen simultaneously with – and as a by-product of – endosymbiosis (Kroemer, 1997). However, it has also been proposed that apoptosis may be the result of the acquisition of the aerobic metabolism by early eukaryotes (Frade & Michaelidis, 1997).

Apoptosis is a unique phenomenon of tissue kinetics as it can be said that life is critically controlled by the operational centre of cell, the nucleus. Instead, death is a process controlled by the power house of the cell, the mitochondria. Thus, even cells lacking nucleus commit apoptosis. In general, the two-step membrane depolarisation and free radical release taking place in the mitochondria may trigger apoptosis. This in fact is not so peculiar if we understand that mitochondria were once free-living bacteria which did not need an external gene control for achieving their functions. Once each came into symbiosis forming a eukaryotic cell, it retained some capacity to operate partially independently.

There are several major apoptotic pathways, but the most well-known and studied are the extrinsic and the intrinsic pathways, which respond to different environmental and cellular challenges in vertebrates. The intrinsic pathway is also called the mitochondrial pathway because of the involvement of mitochondria. There are mitochondrial proteins that induce this process (proapoptotic) and others that limit cell death (antiapoptotic). Both proteins interact so as to cooperate and govern the cell's fate. Also, the origin of the activation signals of apoptosis taking place on the mitochondria is a clue molecule, cytochrome C (Cyt C), which is released from the mitochondria to form the apoptosome complex. The intrinsic pathway – with some differences – is a mostly conserved pathway among metazoans (for a comprehensive review look at Wang & Youle, 2009). Cyt C is a key component of the apoptosome complex for activating the initiator caspase-9 after its release from mitochondria. Under non-apoptotic conditions, Cyt C is kept inside the respiratory chain. Against some cellular challenges, like the alteration of the DNA in the mitochondria or the nucleus, Cyt C is released from its membrane, crossing the external membrane and initiating the formation of the apoptosome complex. In essence, mitochondrial proteins – like Cyt C and caspases – are not hired guns and during non-apoptotic conditions they are responsible for various basic mitochondrial roles for normal cell functioning. The compartmentalisation of such mitochondrial proteins isolates them from interacting with partners or targets, a mechanism to prevent the unwanted activation of apoptosis in normal cells. Only after their appropriate release into the cytoplasm do such proteins play the role of triggers to initiate the cell's suicide.

The classical invertebrate model organisms for the study of apoptosis are *C. elegans* and *Drosophila*. In spite of the fact that the regulators of apoptosis have been found in such model organisms, the involvement of mitochondria in apoptosis is not conclusive. So far, no irrefutable evidence of the release of Cyt C from the intermembrane space has been found. Also, the involvement of Cyt C in the apoptosome formation in *Drosophila* is controversial, and some evidence suggests that Cyt C is not necessary (Rolland & Conradt, 2006).

The current evidence indicates that the whole process of apoptosis -including the involved proteins and the regulation mechanisms- in crustaceans is far more diverse than has been assumed from the studies with model organisms. Recent studies have shown that several proteins in the apoptotic network are quite conserved between mammals and arthropods; however, it is clear that the integration of such homologous proteins in the physiology and pathophysiology of crustaceans needs further experimental assessment. Some unresolved questions regarding this topic are: how does the regulation of the process occur? Is

crustacean apoptosis transcriptionally regulated, as in *Drosophila* (RHG ´killer´ proteins)? Or is it controlled by pro- and anti-apoptotic Bcl-2 family proteins, as in vertebrates? The issues that should be investigated in the short-term are whether the calcium-induced opening of the mitochondrion permeability transition pore (MPTP), commonly found on vertebrate species, also occurs in crustaceans. Furthermore, the study of the differences in the regulation of the intrinsic pathway of crustacean apoptosis will lead to an understanding of their adaptation to challenging environments; this is because marine organisms have to deal with seasonal as well as circadian changes in environmental variables. Some examples are UV radiation, temperature and dissolved oxygen, and even some biological stresses such as toxins that may vary over time. But this is not all: other variables that may inhibit apoptosis must be considered. "Characterisation of the players, pathways, and their significance in the core machinery of crustacean apoptosis is revealing new insights for the field of cell death"(Menze et al., 2010).

Apoptosis is a key host response to viral infection. Viruses that can modulate a host's apoptotic responses are likely to gain important opportunities for transmission. Here, we review recent studies that demonstrate that the particles of Invertebrate Iridescent Virus6 (IIV-6) (Iridoviridae, genus Iridovirus), or an IIV-6 virion protein extract, are capable of inducing apoptosis in lepidopteran and coleopteran cells, at concentrations 1000-fold lower than that required to shut-off the host's macromolecular synthesis (Williams et al., 2009). Throughout the process of pathogen–host coevolution, viruses have developed a battery of distinct strategies to overcome the biochemical and immunological defences of the host. Thus, viruses have acquired the capacity to subvert host cell apoptosis, control inflammatory responses, and evade immune reactions. Since the elimination of infected cells via programmed cell death is one of the oldest defence mechanisms against infection, disabling host cell apoptosis might represent an almost obligatory step in the viral life cycle. Conversely, viruses may take advantage of stimulating apoptosis, either to kill uninfected cells from the immune system or else to induce the breakdown of infected cells, thereby favouring viral dissemination (Galluzzi et al., 2008).

7. Conclusion and future perspectives

As stated by Van der Giezen in 2009 "over the last 5–10 years, it has become apparent that the organelle known as the mitochondrion is a much more fluid entity than generally believed," so "why should mitochondrion be the same in all eukaryotes while other cellular structures show such great evolutionary malleability?"

It is our belief that since natural selection has given invertebrates the opportunity to evolve in quick steps, a large window is opening in the field of mitochondrial research among these species, giving an outstanding opportunity to researchers to contribute to an increase in knowledge, not only because there is scarce information, but also because many species have shown special and unique characteristics that need to be explained.

At this point, the information reviewed clearly shows that invertebrates display remarkable physiological capabilities, including highly specialised mechanisms for adjusting mitochondrial functions to solve their energetic demands under the stressful conditions they usually face. These species also include within their systems ancient and novel molecules and structures acting to reach an adaptive state, from the increasing number of mitochondria per cell to the highly complex function of the HIF system.

It is also remarkable that the number of invertebrate species considered as potential models in the study of mitochondrial function has increased. New data on marine invertebrates, such as molluscs and crustaceans and non-*Drosophila* species, are emerging. Since there is still an immense lack of knowledge about invertebrates, important efforts in new animal models should focus on i) the description of mitochondrial systems in species inhabiting extreme environments, ii) the recognition and understanding of the causes and effects of mitochondrial disorders, and iii) the development of unsolved phylogenetic relationships among species and phyla. This may also open important opportunities for new biotechnological applications to better face the effects of global changes such as warming, hypoxic conditions and chronic stressors that specifically affect the central metabolic pathways in such species.

If the regulation of apoptosis in crustaceans is as varied as their diversity as a species, or at least their Families, then the potential for discovering novel biomolecules is immense. Such molecules may find uses in biotechnologies across diverse industries, including pharmacology. We endorse the hypothesis that an advanced knowledge in apoptosis will provide some clues about how crustaceans deal with viral infections and enable the proposal of feasible strategies to protect farmed crustaceans.

8. References

Abe, H.; Hirai, S. & Okada, S. (2007). Metabolic Responses and Arginine kinase Expression under Hypoxic stress of the Kuruma prawn *Marsupenaeus japonicus*. *Comparative Biochemistry and Physiology. Part A,* Vol.146, No.1, (January 2007), pp. 40-46, ISSN 0300-9629.

Abele, D. & Puntarulo, S. (2004). Formation of Reactive Species and Induction of Antioxidant Defence Systems in Polar and Temperate Marine Invertebrates and Fish. *Comparative Biochemistry and Physiology Part A*, Vol. 138, No. 4, pp. 405-415, ISSN 0300-9629.

Abele, D.; Phillip, E.; Gonzalez, P.M. & Puntarulo, S. (2007). Marine Invertebrate Mitochondria and Oxidative Stress. *Frontiers in Bioscience*, Vol.12, (January 2007), pp. 933-946, ISSN 1093-9946.

Arndt, A & Smith, M.J. (1998). Mitochondrial Gene Rearrangement in the Sea Cucumber Genus Cucumaria. *Molecular Phylogenetics and Evolution*, Vol.15, No.8, (August 1998), pp. 1009-1016, ISSN 1055-7903.

Asakawa, S.; Himeno, H.; Miura, K. & Watanabe, K. (1995). Nucleotide Sequence and Gene Organization of the Starfish *Asterina pectinifera* Mitochondrial Genome. *Genetics*, Vol.140, (July 1995), pp.1047-1060, ISSN 0016-6731.

Ballard, J.W.O. & Melvin, R.G. (2007). Tetracycline Treatment Influences Mitochondrial Metabolism and mtDNA Density two Generations after Treatment in Drosophila. *Insect Molecular Biology*, Vol.16, No.6, (December 2007), pp. 799–802, ISSN 0962-1075.

Banaji, M. (2006). A Generic Model of Electron Transport in Mitochondria. *The Journal of Theoretical Biology*, Vol.243, No.4, (December 2009), pp. 501-516, ISSN 0022-5193.

Barger, J.L.; Brand, M.D.; Barnes, B.M., & Boyer, B.B. (2003). Tissue-Specific Depression of Mitochondrial Proton Leak and Substrate Oxidation in Hibernating Arctic ground Squirrels. *American Journal of Physiology Regulatory, Integrative and Comparative Physiology*, Vol.284, No.5, (May 2003), pp. R1306–R1313, ISSN 0363-6119.

Beaton, M.J.; Roger, A.J. & Cavalier-Smith, T. (1998). Sequence Analysis of the Mitochondrial Genome of *Sarcophyton glaucum*: Conserved Gene Order Among Octocorals. *Journal of Molecular Evolution*, Vol.47, No.6, (December 1998), pp. 697-708, ISSN 0022-2844.

Belevich, I.; Gorbikova, E.; Belevich, N. P.; Rauhamäki, V.; Wikström, M. & Verkhovsky, M. I. (2010). Initiation of the Proton Pump of Cytochrome c Oxidase. *Proceedings of the National Academy of Sciences U.S.A.*, Vol.107, No.43, (October 2010), pp. 18469-18474, ISSN 1091-6490.

Belinky, F.; Rot, C.; Ilan, M. & Huchon, D. (2008). The Complete Mitochondrial Genome of the Demosponge *Negombata magnifica* (Poecilosclerida). *Molecular Phylogenetics and Evolution*, Vol.47, No.3, (January 2008), pp. 1238-43, ISSN 1055-7903.

Bessho, Y.; Ohama, T. & Osawa, S. (1992). Planarian mitochondria II. The Unique Genetic Code as Deduced from Cytochrome c Oxidase Subunit I Gene Sequences. *Journal of Molecular Evolution*, Vol.34, No.4, (April 1992), pp. 331-335, ISSN 0022-2844.

Boore, J.L. & Brown, W.M. (1995). Complete DNA Sequence of the Mitochondrial Genome of the Annelid Worm, *Lumbricus terrestris*. *Genetics,* Vol.141, No.1, (September 1995), pp. 305-319, ISSN 0016-6731.

Boore, J.L; Collins, T.M.; Stanton, D.; Daehler, L.L.; Brown, W.M. (1995). Deducing the Pattern of Arthropod Phylogeny from Mitochondrial DNA Rearrangements. *Nature*, Vol.376, No.6536, (July 1995), pp.163-165, ISSN 0028-0836.

Boore, J.L. (1999). Animal Mitochondrial Genomes. *Nucleic Acids Research*, Vol.27, No.8, (April 1999), pp. 1767-1780, ISSN 0305-1048.

Boore, J.L. & Brown, W.M. (2000). Mitochondrial Genomes of *Galathealinum*, *Helobdella*, and *Platynereis*: Sequence and Gene Arrangement Comparisons Indicate that Pogonophora is not a Phylum and Annelida and Arthropoda are not Sister Taxa. *Molecular Phylogenetics and Evolution*, Vol.17, No.1, (January 2000), pp. 87-106, ISSN 1055-7903.

Boyer, P.D. (1997). The ATP synthase- A Splendid Molecular Machine. *Annual Review of Biochemistry*, Vol.66, (May 1995), pp. 717–749. ISSN 0066-4154.

Brouwer, M.; Brown-Peterson, N.J.; Hoexum-Brouwer, T.; Manning, S. & Denslow, N. (2008). Changes in Mitochondrial Gene and Protein Expression in Grass shrimp, *Palaemonetes pugio*, Exposed to Chronic Hypoxia. *Marine Environmental Research*, Vol.66, No.1, (July 2008), pp. 143-145, ISSN 0141-1136.

Burgents, J.E.; Brunett, K.G. & Burnett, L.E. (2005). Effects of Hypoxia and Hypercapnic Hypoxia on the Localization and the Elimination of *Vibrio campbellii* in *Litopenaeus vannamei*, the Pacific White Shrimp. *Biological Bulletin,* Vol.208, No.3, (June 2005), pp.159-168, ISSN 0006-3185.

Cai, X.Q.; Liu, G.H.; Song, H.Q.; Wu, C.Y.; Zou, F.C.; Yan, H.K.; Yuan, Z.G.; Lin, R.Q. & Zhu, X.Q. (2011). Sequences and Gene Organization of the Mitochondrial Genomes of the Liver Flukes *Opisthorchis viverrini* and *Clonorchis sinensis* (Trematoda). *Parasitology Research*, (May 2011), ISSN (electronic) 1432-1955.

Cardol, P.; Gonzalez-Halphen, D.; Reyes-Prieto, A.; Baurain, D.; Matagne, R. F. & Remacle, C. (2005). The Mitochondrial Oxidative Phosphorylation Proteome of *Chlamydomonas reinhardtii* Deduced from the Genome Sequencing Project. *Plant Physiology*, Vol.137, No.2, (February 2005), pp. 447–459, ISSN 0032-0889.

Chamberlin, M.E. (2004). Control of Oxidative Phosphorylation during Insect Metamorphosis. *American Journal of Physiology- Regulatory, Integrative and Comparative Physiology*, Vol.287, No.2, (April 2004), pp. R314-R321, ISSN 0363-6119.

Chen, H. & Chan, D.C. (2009). Mitochondrial Dynamics–Fusion, Fission, Movement, and Mitophagy–in Neurodegenerative Diseases. *Human Molecular Genetics,* Vol.18, No.2, (October 2009), pp. R169–R176, ISSN 0964-6906.

Cheng, R.; Zheng, X.; Lin, Z.; Yang, J. & Li, Q. (2011). Determination of the Complete Mitochondrial DNA Sequence of *Octopus minor*. *Molecular Biology Reports*, (June 2011) On line version. ISSN (electronic) 1573-4978.

Clary, D.O. & Wolstenholme, D.R. (1985). The Mitochondrial DNA Molecule of *Drosophila yakuba*: Nucleotide Sequence, Gene Organization and the Genetic Code, *Journal of Molecular Evolution*, Vol.22, No.3, (February 1986), pp. 252-271, ISSN 0022-2844.

Clavero-Salas,A.; Sotelo-Mundo, R.; Gollas-Galván, T.; Hernandez-Lopez, J.; Peregrino-Uriarte, A.; Muhlia-Almazán, A.; Yepiz-Plascencia, G. (2007). Transcriptome Analysis of Gills from the White Shrimp *Litopenaeus vannamei* Infected with White Spot Syndrome Virus. *Fish & Shellfish Immunology*, Vol.23, No.2, (August 2007), pp. 459-472, ISSN 1050-4648.

Crozier, R.H. & Crozier, Y.C. (1993). The Mitochondrial Genome of the Honeybee *Apis mellifera*: Complete Sequence and Genome Organization. *Genetics*, Vol.133, No.1, (January 1993), pp. 97-117, ISSN 0016-6731.

Dall, W.; Hill, B.J.; Rothlisberg, P.C. & Staples, D.J. (1990). The Biology of Penaeidae, In: *Advances in Marine Biology*, J.H.S. Blaxter & A.J. Southward, (Ed.), 1-488, Academic Press, ISBN 0-12-026127-8, San Diego, CA.

Das, S.; Radtke, A.; Choi, Y.J.; Mendes, A.M.; Valenzuela, J.G. & Dimopoulos, G. (2010). Transcriptomic and Functional Analysis of the *Anopheles gambiae* Salivary Gland in Relation to Blood Feeding. *BMC Genomics*, Vol.566, (October 2010), pp. 566, ISSN 1471-2164.

Davila, S.; Piñero, D.; Bustos, P.; Cevallos, M.A. & Davila, G. (2005). The Mitochondrial Genome Sequence of the Scorpion *Centruroides limpidus* (Karsch 1879) (Chelicerata; Arachnida). *Gene*, Vol.360, No.2, (November 2005), pp. 92-102, ISSN 0378-1119.

de Oliveira, U.O.; da Rosa-Araujo, A.S.; Bello-Klein, A.; da Silva, R.S.M & Kucharski, L.C. (2005). Effects of Environmental Anoxia and Different Periods of Reoxygenation on Oxidative Balance in Gills of the Estuarine Crab *Chasmagnathus granulata*. *Comparative Biochemistry and Physiology. Part B,* Vol.140, No.1, (January 2005), pp. 51-57, ISSN 1096-4959.

Diaz, R.J. (2001). Overview of Hypoxia around the World. *Journal of Environmental Quality*, Vol.30, No.2, (March-April 2001), pp. 275-281, ISSN 0047-2425.

Diaz, F. (2010). Cytochrome c Oxidase Deficiency: Patients and Animal Models. *Biochimica et Biophysica Acta*, Vol.1802, No.10, (January 2010), pp. 100-110, ISSN 0925-4439.

Dirnagl, U.; Becker, K. & Meisel, A. (2009). Preconditioning and Tolerance Against Cerebral Ischaemia: from Experimental Strategies to Clinical Use. *Lancet Neurology*, Vol.8, No.4, (April 2009), pp. 398–412, ISSN 1474-4422.

Di Simplicio, P.; Rossi, R.; Falcinelli, S.; Ceserani, R. & Formento, M.L. (1997). Antioxidant Status in Various Tissue of the Mouse after Fasting and Swimming Stress. *European Journal of Applied Physiology*, Vol.76, No.4, pp.302-307, ISSN 0301-5548.

Driscoll, M. & Gerstbrein, B. (2003). Dying for a Cause: Invertebrate Genetics Takes on Human Neurodegeneration. *Nature Reviews*, Vol.4, No.3, (March 2003), pp. 181-194, ISSN 471-0056.

Dudkina N.; Sunderhaus, S.; Boekema, E. & Braun, H. (2008). The Higher Level of Organization of the Oxidative Phosphorylation System: Mitochondrial Supercomplexes. *Journal of Bioenergetics and Biomembranes*. Vol.40, No.5, (October 2008), pp. 419-424. ISSN 1573-6881.

Dudkina, N. V.; Kouril, R.; Peters, K.; Braun, H.P. & Boekema, E.J. (2010). Structure and Function of Mitochondrial Supercomplexes. *Biochimica et Biophysica Acta*, Vol.1797, No.6-7, (June-July 2010), pp. 664-70, ISSN 0006-3002.

Durieux, J.; Wolff, S. & Dillin, A. (2011). The Cell-Non-Autonomous Nature of Electron Transport Chain-Mediated Longevity. *Cell*, Vol.144, No.1, (January 2011), pp. 79–91, ISSN 0092-8674.

Eads, B.D. & Hand, S.C. (1999). Regulatory Features of Transcription in Isolated Mitochondria from *Artemia franciscana* Embryos. *American Journal of Physiology*, Vol.277, No.6, (December 1999), pp. R1588-R1597, ISSN 0363-6119.

Eads, B.D. & Hand, S.C. (2003). Mitochondrial mRNA Stability and Polyadenylation during Anoxia-Induced Quiescence in the Brine Shrimp *Artemia franciscana. The Journal of Experimental Biology,* Vol.206, No.20, (October 2003), pp. 3681-3692, ISSN 0022-0949.

Ellington, C.P. (1985). Power and Efficiency of Insect Flight Muscle. *The Journal of Experimental Biology*, Vol.115, (March 1985), pp. 293-304, ISSN 0022-0949.

Ellington, W.R. & Hines, A.C. (1991). Mitochondrial Activities of Phosphagen Kinases are not Widely Distributed in the Invertebrates. *The Biological Bulletin,* Vol.180, No.3, (June 1991), pp. 505-507, ISSN 1062-3590.

English, T.E. & Storey, K.B. (2003). Freezing and Anoxia Stresses Induce Expression of Metallothionein in the Foot Muscle and Hepatopancreas of the Marine Gastropod *Littorina littorea. The Journal of Experimental Biology*, Vol.206, No.14, (July 2003), pp. 2517-24, ISSN 0022-0949.

Falkenberg, M.; Larsson, N.G. & Gustafsson, C.M. (2005). DNA Replication and Transcription in Mammalian Mitochondria. *Annual Review of Biochemistry*, Vol.76, (July 2007), pp. 679-699, ISSN 0066-4154.

Figueroa, P.; Leon, G.; Elorza, A.; Holuigue, L.; Araya, A. and Jordana, X. (2002). The Four Subunits of Mitochondrial Respiratory Complex II are encoded by Multiple Nuclear Genes and Targeted to Mitochondria in *Arabidopsis thaliana. Plant Molecular Biology*, Vol. 50, No. 4-5, (Noviember 2002), pp. 725-734, ISSN 0735-9640.

Fontanesi, F.; Soto, I. & Barrientos, A. (2008). Cytochrome c Oxidase Biogenesis: New Levels of Regulation. *The International Union of Biochemistry and Molecular Biology*, Vol.60, No.9, (September 2008), pp. 557-568, ISSN 1521-6543.

Frade, J. M. & Michaelidis, T. M. (1997). Origin of Eukaryotic Programmed Cell Death: A Consequence of the Aerobic Metabolism. *BioEssays*, Vol.19, No. 9, (September 1997), pp. 827-832, ISSN 0265-9247.

Fridell, Y.-W.; Sanchez-Blanco, A.; Silvia, B.A. & Helfand, S.L. (2004). Functional Characterization of a Drosophila Mitochondrial Uncoupling Protein. *Journal of Bioenergetics and Biomembranes*. Vol. 36, No. 3, (June, 2004), pp. 219-228, ISSN 1573-6881.

Friedrich, T. & Weiss, H. (1997). Modular Evolution of the Respiratory NADH: Ubiquinone Oxidoreductase and the Origin of its Molecules. *The Journal of Theoretical Biology*. Vol.187. (September 1997). pp 529-540, ISSN 0022-5193.

Galluzzi L.; Brenner, C.; Morselli, E.; Touat, Z. & Kroemer, G. (2008). Viral Control of Mitochondrial Apoptosis. *PLoS Pathogens*, Vol.4, No.5, (May 2008), ISSN 1553-7366.

Garcia-Orozco, K.D.; Aispuro-Hernandez, E.; Yepiz-Plascencia, G.; Calderon-de-la Barca, A.M. & Sotelo-Mundo, R. (2007). Molecular Characterization of Arginine Kinase, an Allergen from the Shrimp *Litopenaeus vannamei*. *International Archives of Allergy and Immunology*, Vol.144, No.1, (May 2007), pp 23-28, ISSN 1018-2438.

Garesse, R. (1988). *Drosophila melanogaster* Mitochondrial DNA: Gene Organization and Evolutionary Considerations. *Genetics*, Vol.118, No.4, (April 1988), pp. 649-663, ISSN 0016-6731.

Genes, C.; Baquero, E.; Echeverri, F.; Maya, J.D. & Triana, O. (2011). Mitochondrial Dysfunction in *Trypanosoma cruzi*: the Role of *Serratia marcescens* Prodigiosin in the alternative Treatment of Chagas Disease. *Parasites & Vectors*, Vol.4, (May 2011), pp. 66, ISSN 1756-3305.

Goodman, W.G.; Carlson, R.O. & Nelson, K.L. (1985). Analysis of Larval and Pupal Development in the Tobacco Hornworm (Lepidoptera: Sphingidae), *Manduca sexta*. *Annals of the Entomological Society of America*, Vol.78, No.1, (January 1985), pp. 70-80, ISSN: 0013-8746.

Grad, L.I.; Sayles, L.C. & Lemire, B.D. (2008). Isolation and Functional Analysis of Mitochondria from the Nematode *Caenorhabditis elegans*. In: *Mitochondria: Practical Protocols*, D. Leister & J.M. Herrmann, (Ed.), Methods in Molecular Biology, Vol.372, 51-66. Humana Press Inc., ISSN 1064-3745, Totowa, NJ. USA.

Gray, M. W.; Burger, G. & Lang, B.F. (1999). Mitochondrial Evolution. *Science*. Vol.283, No.5407, (March 1999), pp.1476-1481, ISSN 0036-8075.

Guerrero-Castillo, S.; Araiza-Olivera, D.; Cabrera-Orefice, A.; Espinasa-Jaramillo, J.; Gutierrez-Aguilar, M.; Luevano-Martinez, l.A.; Zepeda-Bastida, A. & Uribe-Carbajal, S. (2011). Physiological Uncoupling of Mitochondrial Oxidative Phosphorylation. Studies in Different Yeast Species. *Journal of Bioenergetics and Biomembranes*, Vol. 43, (May 2010), pp. 323-331, ISSN1573-6881.

Guzy, R.D.; Mack, M.M. & Schumacker, P.T. (2007). Mitochondrial Complex III is required for Hypoxia-induced ROS Production and Gene Transcription in Yeast. *Antioxidants and Redox Signaling*, Vol.9, No.9, (September 2007), pp. 1317-1328, ISSN 1523-0864.

Hakkaart, G. A.; Dassa, E. P.; Jacobs, H. T. & Rustin, P. (2006). Allotropic Expression of a Mitochondrial Alternative Oxidase Confers Cyanide Resistance to Human Cell Respiration. *EMBO Reports*, Vol.7, No.3, (March 2006), pp. 341-5, ISSN 1469-221X

Hand, S.C. (1998). Quiescence in *Artemia franciscana* Embryos: Reversible Arrest of Metabolism and Gene Expression at low Oxygen Levels. *The Journal of Experimental Biology*, Vol.201, No.8, (April 1988), pp. 1233–1242, ISSN 0022-0949.

Hahlbeck, E.; Arndt, C. & Schiedek, D. (2000). Sulphide Detoxification in *Hediste diversicolor* and *Marenzelleria viridis*, Two Dominant Polychaete Worms within the Shallow Coastal Waters of the Southern Baltic Sea. *Comparative Biochemistry and Physiology Part B*, Vol.125, No.4, (April 2000), pp. 457-71, ISSN 1096-4959.

Harrison, J.F. & Roberts, S.P. (2000). Flight Respiration and Energetics. *Annual Review of Physiology*, Vol.62, (March 2000), pp. 179-205, ISSN 0066-4278.

He, N.; Qin, Q. & Xu, X. (2005). Differential Profile of Genes Expressed in Haemocytes of White Spot Syndrome Virus-Resistant Shrimp (*Penaeus japonicus*) by Combining Suppression Subtractive Hybridization and Differential Hybridization, *Antiviral Research*, Vol.66, No.1, (April 2005), pp. 39-45, ISSN 0166-3542.

Hengarter, M.O. (2000). The Biochemistry of Apoptosis. *Nature*, Vol.40, No.6805, (October 2000), pp. 770-776, ISSN 0028-0836.

Hervant, F. & Renault, D. (2002). Long-term Fasting and Realimentation in Hypogean and Epigean Isopods: A Proposed Adaptive Strategy for Groundwater Organisms. *The Journal of Experimental Biology*, Vol.205, No.14, (July 2002), pp. 2079-2087, ISSN 0022-0949.

Himeno, H.; Masaki, H.; Ohta, T.; Kumagai, I.; Miura, K.I. & Watanabe, K. (1987). Unusual Genetic Codes and a Novel Genome Structure for tRNA SerAGY in Starfish Mitochondrial DNA. *Gene*, Vol.56, No.2-3, pp. 219-230, ISSN 0378-1119.

Hird, F.J. (1986). The Importance of Arginine in Evolution. *Comparative Biochemistry and Physiology. Part B*, Vol.8, No.2, pp. 285-8, ISSN 0305-0491.

Hochachka, P.W. & Somero, G.N. (2002). Influence of Oxygen Availability, In: *Biochemical Adaptation,* P.W. Hochachka &, G.N. Somero, (Ed.), 107-157, Oxford University Press, ISBN 0-19-511702-6, NY, USA.

Hoffmann, R.J.; Boore J, L. & Brown W.M. (1992). A Novel Mitochondrial Genome Organization for the Blue Mussel *Mytilus edulis*. *Genetics*, Vol.131, No.2, (June 1992), pp. 397-412, ISSN 0016-6731.

Hu, M.; Chilton, N.B. & Gasser, R.B. (2002). The Mitochondrial Genomes of the Human Hookworms, *Ancylostoma duodenale* and *Necator americanus* (Nematoda: Secernentea). *International Journal for Parasitology*. Vol.32, No.2, (February 2002), pp. 145-58, ISSN 0020-7519.

Huang, J. & Lemire, B.D. (2009). Mutations in the *C. elegans* Succinate Dehydrogenase Iron-Sulfur Subunit Promote Superoxide Generation and Premature Aging. *Journal of Molecular Biology*, Vol.387, No.3, (April 2009), pp. 559-569, ISSN 0022-2836.

Itoi, S.; Kinoshita, S.; Kikuchi, K. & Watabe, S. (2003). Changes of Carp FoF_1-ATPase in Association with Temperature Acclimation. *American Journal of Physiology - Regulatory, Integrative and Comparative Physiology*, Vol.284, No.1, (September 2002), pp. R153–R163, ISSN 0363-6119.

Jacobs, H.T.; Elliott, D.J.; Math, V.B. & Farquharson, A. (1988). Nucleotide Sequence and Gene Organization of Sea Urchin Mitochondrial DNA. *Journal of Molecular Evolution*. Vol.202, No.2, (July 1988), pp.185-217, ISSN 0022-2844.

Jiang, W. & Wang, X. (2004). Cytochrome C-Mediated Apoptosis. *Annual Review of Biochemistry*, Vol.73, (July 2004), pp. 87-106, ISSN 0066-4154.

Jiang, S.T.; Hong, G.Y.; Yu, M.; Li, N.; Yang, Y.; Liu, Y.Q. & Wei, Z.J. (2009). Characterization of the Complete Mitochondrial Genome of the Giant Silkworm Moth, *Eriogyna pyretorum* (Lepidoptera: Saturniidae). *International Journal of Biological Sciences*, Vol.5, No.4, (May 2009), pp. 351-365, ISSN 1449-2288.

Jubrias, S.A.; Esselman, P.C.; Price, L.B.; Cree, M.E. & Conley, K.E. (2001). Large energetic Adaptations of Elderly Muscle to Resistance and Endurance Training. *Journal of Applied Physiology,* Vol.90, No.5, (May 2001), pp. 1663-1770, ISSN 0363-6143.

Julian, D.; Dalia, W.E. & Arp, A. (1998). Neuromuscular Sensitivity to Hydrogen Sulfide in the Marine Invertebrate *Urechis caupo*. *The Journal of Experimental Biology*, Vol.201, No.9, (May 1998), pp. 1393-1403, ISSN 0022-0949.

Kayal, E. & Lavrov, D.V. (2008). The Mitochondrial Genome of *Hydra oligactis* (Cnidaria, Hydrozoa) Sheds New Light on Animal mtDNA Evolution and Cnidarian Phylogeny. *Gene*, Vol.410, No.1, (February 2008), pp. 177-186, ISSN 0378-1119.

Keddie, E.M.; Higazi, T. & Unnasch, T.R. (1998). The Mitochondrial Genome of *Onchocerca volvulus*: Sequence, Structure and Phylogenetic Analysis. *Molecular and Biochemical Parasitology*, Vol.95, No.1, (September 1998), pp. 111–127, ISSN 0166-6851.

Kern, B.; Ivanina, A.V.; Piontkivska, H.; Sokolov, E.P. & Sokolova, I.M. (2009). Molecular Characterization and Expression of a Novel Homolog of Uncoupling Protein 5 (UCP5) from the Eastern Oyster *Crassostrea virginica* (Bivalvia: Ostreidae). *Comparative Biochemistry and Physiology Part D*, Vol.4, No.2, (June 2009), pp. 121-127, ISSN 744-117X.

Khalimonchuk, O. & Rödel, G. (2005). Biogenesis of Cytochrome c Oxidase. *Mitochondrion*, Vol.5, No.6, (December 2005), pp. 363-388, ISSN 1567-7249.

Kidd, T.; Abu-Shumays, R.; Katzen, A.; Sisson, J.C.; Jimenez, G.; Pinchin, S.; Sullivan, W. & Ish-Horowicz, D. (2005). The Epsilon-subunit of Mitochondrial ATP synthase is Required for Normal Spindle Orientation during the Drosophila Embryonic Divisions. *Genetics,* Vol. 170, No.2, (June 2005), pp. 697-708, ISSN 0016-6731.

Klimova, T. & Chandel, N.S. (2008). Mitochondrial Complex III Regulates Hypoxic Activation of HIF. Cell Death and Differentiation. Vol. 15, (January 2008), pp 660-666, ISSN 1350-9047.

Kotlyar, S.; Weihrauch, D.; Paulsen, R. & Towle, D.W. (2000). Expression of Arginine Kinase Enzymatic Activity and mRNA in Gills of the Euryhaline Crabs *Carcinus maenas* and *Callinectes sapidus. The Journal of Experimental Biology.* Vol.203, (July 2000), pp. 2395-2404, ISSN 0022-0949.

Kroemer, G. (1997). Mitochondrial Implication in Apoptosis. Towards an Endosymbiont Hypothesis of Apoptosis Evolution. *Cell Death & Differentiation*, Vol. 4, No. 6, (August 1997), pp. 443-456, ISSN 1350-9047.

Lai-Zhang, J. & Mueller, D. (2000). Complementation of Deletion Mutants in the Genes Encoding the F1- ATPase by Expression of the Corresponding Bovine Subunits in Yeast *S. cerevisiae. European Journal of Biochemistry*, Vol.267, No.8, (April 2000), pp. 2409-2418, ISSN 0014-2956.

Lavrov, D.V.; Wang, X. & Kelly, M. (2008). Reconstructing Ordinal Relationships in the Demospongiae Using Mitochondrial Genomic Data. *Molecular Phylogenetics and Evolution*. Vol.49, No.1, (October 2008), pp. 111-24, ISSN 1055-7903.

Lee, S.S.; Lee, R.Y.N.; Fraser, A.G.; Kamath, R.S.; Ahringer, J. & Ruvkun, G. (2003). A Systematic RNAi Screen Identifies a Critical Role for Mitochondria in *C. elegans* Longevity. *Nature Genetics*, Vol.33, No.1, (January 2003), pp. 40–48, ISSN 1061-4036.

Lee, S.J.; Hwang, A.B. & Kenyon, C. (2010). Inhibition of Respiration Extends *C. elegans* Life Span via Reactive Oxygen Species that Increase HIF-1 Activity. *Current Biology*, Vol.20, No.23, pp.2131-2136, ISSN 0960-9822.

Levy, O.; Kaniewska, P.; Alon, S.; Eisenberg, E.; Karako-Lampert, S.; Bay, L.K.; Reef, R.; Rodriguez-Lanetty, M.; Miller, D.J. & Hoegh-Guldberg, O. (2011). Complex Diel

Cycles of Gene Expression in Coral-Algal Symbiosis. *Science*, Vol.331, No.6014, (January 2011), pp. 175, ISSN 0036-8075.

Li, T. & Brouwer, M. (2009). Gene Expression Profile of the Grass Shrimp *Palaemonetes pugio* Exposed to Chronic Hypoxia. *Comparative Biochemistry and Physiology Part D,* Vol.4, No.3, (September 2009), pp. 196-208, ISSN 1744-117X.

Li, Z. & Neufeld, G.J. (2001a). Isolation and Characterization of Mitochondrial F(1)-ATPase from Crayfish (*Orconectes virilis*) Gills. *Comparative Biochemistry and Physiology. Part B*, Vol.128, No.2, (February 2001), pp. 325-338, ISSN 1096-4959.

Li, Z. & Neufeld, G.J. (2001b). Kinetic Studies on Mitochondrial F(1)-ATPase from Crayfish (*Orconectes virilis*) Gills. *Comparative Biochemistry and Physiology. Part B*, Vol.128, No.2, (February 2001), pp. 339-350, ISSN 1096-4959.

Liang, Y.; Cheng, J.J.; Yang, B. & Huang, J. (2010). The Role of F1 ATP synthase Beta Subunit in WSSV Infection in the Shrimp, *Litopenaeus vannamei. Virology Journal*, Vol.7, (June 2010), pp. 144, ISSN 1098-5514.

Liu, G.H.; Lin, R.Q.; Li, M.W.; Liu, W.; Liu, Y.; Yuan, Z.G.; Song, H.Q.; Zhao, G.H.; Zhang, K.X. & Zhu, X.Q. (2011). The Complete Mitochondrial Genomes of Three Cestode Species of *Taenia* Infecting Animals and Humans. *Molecular Biology Reports*, Vol.38, No.4, (April 2011), pp. 2249-56, ISSN 0301-4851.

Mao, X. R. & Crowder, C.M. (2010). Protein Misfolding Induces Hypoxic Preconditioning via a subset of the Unfolded Protein Response Machinery. *Molecular and Cellular Biology*, Vol.30, No.21, (November 2010), pp. 5033-42, ISSN 0270-7306.

Martinez-Cruz, O. (2007). Expresion Genica de las Subunidades atp6 Mitocondrial y atpc Nuclear del Complejo ATP-Sintasa en el Camaron Blanco (*Litopenaeus vannamei*) en Condiciones de Hipoxia. Master of Science Thesis. Centro de Investigacion en Alimentacion y Desarrollo, A.C. Hermosillo, Sonora. pp. 1-55.Mexico.

Martinez-Cruz, O.; Garcia-Carreño, F.; Robles-Romo, A.; Varela-Romero, A. & Muhlia-Almazan, A. (2011). Catalytic Subunits *atp*α and *atp*β from the Pacific White shrimp *Litopenaeus vannamei* FoF_1 ATP-synthase complex: cDNA Sequences, Phylogenies, and mRNA Quantification During Hypoxia. *Journal of Bioenergetics and Biomembranes*, Vol.43, (March 2011), pp. 119-133, ISSN 1573-6881.

Martinez–Cruz, O.; Arvizu-Flores, A.; Sotelo-Mundo, R.; Garcia-Carreño, F.; Yepiz-Plascencia, G. & Muhlia-Almazan, A. (2011). Molecular Characterization and Relative Expression of the F1 Subunits from the Mitochondrial ATP-synthase Complex in the Tail Muscle of the White Shrimp *Litopenaeus vannamei* During Hypoxia. In Preparation.

Mattisson, A.G.M. (1965). The Localization of Succinic Dehydrogenase in the Muscles of *Nereis virens* and *Homarus gammarus*. *Histochemistry and Cell Biology*, Vol.5, No.5, (June 1965), pp. 97-115, ISSN 0948-6143.

Mayevsky A. & Rogatsky, G. (2007). Mitochondrial Function *in vivo* Evaluated by NADH Fluorescence: from Animal Models to Human Studies. *American Journal of Physiology - Cell Physiology,* Vol.292, No.2, (February 2007), pp. C615-C640, ISSN 0363-6143.

McDonald, A.E.; Vanlerberghe, G.C. & Staples, J.F. (2009). Alternative Oxidase in Animal: Unique Characteristics and Taxonomic Distribution. *The Journal of Experimental Biology*, Vol.212, (August 2009), pp. 2627-2634, ISSN 0022-0949.

Menze, M.A.; Fortner, G.; Nag, S. & Hand, S.C. (2010). Mechanisms of Apoptosis in Crustacea: What Conditions Induce Versus Suppress Cell Death? *Apoptosis: an International Journal on Programmed Cell Death,* Vol.15, No.3, (March 2010), pp. 293-312, ISSN 1360-8185.

Mitchell, P. (1976). Possible Molecular Mechanisms of the Protonmotive Function of Cytochrome Systems. *The Journal of Theoretical Biology,* Vol.62, No.2, (October 1976), pp. 327-367, ISSN 0022-5193.

Moraes, C.T. (2001). What Regulates Mitochondrial DNA Copy Number in Animal Cells? *TRENDS in Genetics*, Vol.17, No.4, (April 2001), pp. 199- 205, ISSN 0168-9525.

Morris, S.; Aardt, W. & Ahern, M. (2005). The Effect of Lead on the Metabolic and Energetic Status of the Yabby, *Cherax destructor* During Environmental Hypoxia. *Aquatic Toxicology*, Vol.75, No.1, (October 2005), pp. 16-31, ISSN 0166-445X.

Mueller, D.M.; Puri, N.; Kabaleeswaran, V.; Terry, C.; Leslie, A.G.W. & Walker J.E. (2004). Ni-chelate-Affinity Purification and Crystallization of the Yeast Mitochondrial F1-ATPase. *Protein Expression and Purification*, Vol.37, No.2, (October 2004), pp. 479-485, ISSN 1046-5928.

Muhlia-Almazan, A.; Martinez-Cruz, O.; Navarrete del Toro, M. A.; Garcia-Carreño, F.; Arreola, R.; Sotelo-Mundo, R. & Yepiz-Plascencia, G. (2008). Nuclear and Mitochondrial Subunits from the White Shrimp *Litopenaeus vannamei* FoF_1 ATP-synthase complex: cDNA Sequence, Molecular Modeling, and mRNA Quantification of *atp9* and *atp6*. *Journal of Bioenergetics and Biomembranes*, Vol.40, No.4, (September 2008), pp. 359–369, ISSN 0145-479X.

Mwinyi, A.; Bailly, X.; Bourlat, S.J.; Jondelius, U.; Littlewood, D.T. & Podsiadlowski, L. (2010). The Phylogenetic position of Acoela as Revealed by the Complete Mitochondrial Genome of *Symsagittifera roscoffensis*. *BMC Evolutionary Biology*, Vol.13, (October 2010), pp. 309, ISSN 1471-2148.

Negrisolo, E.; Minelli, A. & Valle, G. (2004). The Mitochondrial Genome of the House Centipede *Scutigera* and the Monophyly Versus Paraphyly of Myriapods. *Molecular Phylogenetics and Evolution*, Vol.21, No.4, (April 2004), pp. 770-780, ISSN 1055-7903.

Nestel, D.; Tomalsky, D.; Rabossi, A. & Quesada-Alllue, L.A. (2003). Lipid, Carbohydrates and Protein Patterns During Metamorphosis of the Mediterranean Fruit Fly, *Ceratitis capitata*, (Diptera: Tephritidae). *Annals of the Entomological Society of America*, Vol.96, No.3, (May 2003), pp. 237-244, ISSN 0013-8746.

Noguchi, Y.; Endo, K.; Tajima, F. & Ueshima, R. (2000). The Mitochondrial Genome of the Brachiopod *Laqueus rubellus*. *Genetics,* Vol.155, No.1, (May 2000), pp. 245-259, ISSN 0016-6731.

Nübel, E.; Wittig, I.; Kerscher, S.; Brandt, U. & Schägger, H. (2009). Two-Dimensional Native Electrophoresis Analysis of Respiratory Supercomplexes from *Yarrowia lipolytica*. *Proteomics*, Vol.9, No.9, (May 2009), pp. 2408-2418, ISSN 1615-9853.

Okimoto, R., Macfarlane, J.L., Clary, D.O. & Wolstenholme, D.R. (1992). The Mitochondrial Genomes of Two Nematodes, *Caenorhabditis elegans* and *Ascaris suum*. *Genetics,* Vol.130, No.3, (March 1992), pp. 471-498, ISSN 0016-6731.

Oleaga, A.; Escudero-Poblacion, A.; Camafeita, E. & Perez-Sanchez, R. (2007). A Proteomic Approach to the Identification of Salivary Proteins from the Argasid Ticks *Ornithodoros moubata* and *Ornithodoros erraticus*. *Insect Biochemistry and Molecular Biology*, Vol.37, No.11, (November 2007), pp. 1149-1159, ISSN 0965-1748.

Peck, L.S. (2002). Ecophysiology of Antarctic Marine Ectotherms: Limits to Life. *Polar Biology*, Vol.25, No.1, (September 2001), pp. 31-40, ISSN 0722-4060.

Pedler, S.; Fuery, C.J.; Withers, P.C.; Flanigan, J. & Guppy, M. (1996). Effectors of Metabolic Depression in an Estivating Pulmonate Snail (*Helix aspersa*): Whole Animal and *in vitro* Tissue Studies. *Journal of Comparative Physiology Part B*, Vol.166, No.6, pp. 375–381, ISSN 0174-1578.

Peregrino-Uriarte, A., Varela-Romero, A., Muhlia-Almazan, A., Anduro-Corona, I., Vega-Heredia, S., Gutierrez-Millan, L., De la Rosa-Velez, J., Yepiz-Plascencia, G. (2009). The Complete Mitochondrial Genomes of the Yellowleg Shrimp *Farfantepenaeus californiensis* and the Blue Shrimp *Litopenaeus stylirostris* (Crustacea: Decapoda). *Comparative Biochemistry and Physiology Part D,* Vol.4, No.1, (March 2009), pp. 45-53, ISSN 1744-117X.

Popova-Butler, A. & Dean, D.H. (2009). Proteomic Analysis of the Mosquito *Aedes aegypti* Midgut Brush Border Membrane Vesicles. *Journal of Insect Physiology*, Vol.55, No.3, (March 2009), pp. 264–272, ISSN: 0022-1910.

Qureshi, S.A. & Jacobs, H.T. (1993). Two Distinct, Sequence-Specific DNA-Binding Proteins Interact Independently with the Major Replication Pause Region of Sea Urchin mtDNA. *Nucleic Acids Research*, Vol.21, No.12, (January 1993), pp. 2801-8, ISSN 0305-1048.

Racotta I.; Palacios, E. & Mendez, L. (2002). Metabolic Responses to Short and Long-Term Exposure to Hypoxia in White Shrimp (*Penaeus vannamei*). *Marine and Freshwater Behaviour and Physiology,* Vol.35, pp. 269-275, ISSN 023-6244.

Ren, J.; Liu, X.; Jiang, F.; Guo, X. & Liu, B. (2010). Unusual Conservation of Mitochondrial Gene Order in *Crassostrea* Oysters: Evidence for Recent Speciation in Asia. *BMC Evolutionary Biology*. Vol.10, (December 2010), pp.394, ISSN 1471-2148.

Rich, P.R. & Marechal, A. (2010). The Mitochondrial Respiratory Chain. *Essays in Biochemistry*. Vol.47, pp.1-27. ISSN 0071-1365.

Ripamonti, M.; Vigano, A.; Moriggi, M.; Milano, G.; von Segesser, L.K.; Samaja, M. & Gelfi, C. (2006). Cytochrome c Oxidase Expression in Chronic and Intermittent Hypoxia Rat Gastrocnemius Muscle Quantitated by CE. *Electrophoresis*, Vol.27, No.19, (October 2006), pp. 3897-3903, ISSN 0173-0835.

Robin, E.D. & Wong, R. (1988). Mitochondrial DNA Molecules and Virtual Number of Mitochondria per Cell in Mammalian Cells. *Journal of Cellular Physiology*, Vol.136, No.3, (September 1988), pp. 507-13, ISSN 0021-9541.

Rolland, S. & Conradt, B. (2006). The Role of Mitochondria in Apoptosis Induction in *Caenorhabditis elegans*: More than Just Innocent Bystanders? *Cell Death and Differentiation*, Vol.13, No.8, (August 2006), pp. 1281–1286, ISSN 1350-9047.

Rosa, R.D. & Barracco, M.A. (2008). Shrimp Interferon is Rather a Portion of the Mitochondrial Fo-ATP Synthase than a True α-interferon. *Molecular Immunology*, Vol.45, No.12, (July 2008), pp. 3490-3493, ISSN 0161-5890.

Rosengarten, R.D.; Sperling, E.A.; Moreno, M.A.; Leys, S.P. & Dellaporta, S.L. (2008). The Mitochondrial Genome of the Hexactinellid Sponge *Aphrocallistes vastus*: Evidence for Programmed Translational Frameshifting. *BMC Genomics*, Vol.9, (January 2008), pp.33, ISSN 1471-2164.

Ryan, M.T. & Hoogenraad, N.J. (2007). Mitochondrial-Nuclear Communications. *Annual Review of Biochemistry*, Vol.76, pp. 701-722, ISSN 0066-4154.

Sanchez-Paz, A.; Garcia-Carreño, F.; Hernandez-Lopez J.; Muhlia-Almazan, A. & Yepiz-Plascencia, G. (2007). Effect of Short-term Starvation on Hepatopancreas and Plasma Energy Reserves of the Pacific White Shrimp (*Litopenaeus vannamei*). *Journal of Experimental Marine Biology and Ecology*, Vol.340, pp. 184-193, ISSN 0022-0981.

Sanchez-Paz, A. (2010). White Spot Syndrome Virus: An Overview on an Emergent Concern. *Veterinary Research*, Vol.41, No.6, (November-December 2010), pp. 43, ISSN 1573-7446.

Sanz, A.; Soikkeli, M.; Portero-Otin, M.; Wilson, A.; Kemppainen, E.; McIlroy, G.; Ellilä, S.; Kemppainen, K.K.; Tuomela, T.; Lakanmaa, M.; Kiviranta, E.; Stefanatos, R.; Dufour, E.; Hutz, B.; Naudi, A.; Jove, M.; Zeb, A.; Vartiainen, S.; Matsuno-Yagi, A.; Yagi, T.; Rustin, P.; Pamplona, R. & Jacobs, H.T. (2010). Expression of the Yeast NADH Dehydrogenase Ndi1 in Drosophila Confers Increased Lifespan Independently of Dietary Restriction. *Proceedings of the National Academy of Sciences, USA,* Vol.107, No.20, (May 2010), pp. 9105–9110, ISSN 1091-6490.

Segovia, R.; Pett, W.; Trewick, S. & Lavrov, D.V. (2011). Extensive and Evolutionarily Persistent Mitochondrial tRNA Editing in Velvet Worms (phylum Onychophora). *Molecular Phylogenetics and Evolution*, (May 2011), ISSN (electronic) 1537-1719.

Seibel, B.A. (2011). Critical Oxygen Levels and Metabolic Suppression in Oceanic Oxygen Minimum Zones. *The Journal of Experimental Biology*, Vol.214, (January 2011), pp. 326-336, ISSN 0022-0949.

Semenza, G.L. (2007). Oxygen-dependent Regulation of Mitochondrial Respiration by Hypoxia-Inducible Factor. *Biochemical Journal*, Vol.405, No.1, (July 2007), pp. 1-9, ISSN 0264-6021.

Shao, Z.; Graf, S.; Chaga, O.Y. & Lavrov, D.V. (2006). Mitochondrial Genome of the Moon Jelly *Aurelia aurita* (Cnidaria, Scyphozoa): A linear DNA Molecule Encoding a Putative DNA-Dependent DNA polymerase. *Gene*, Vol.381, (October 2006), pp. 92-101, ISSN 0378-1119.

Shen, X.; Ren, J.; Cui, Z.; Sha, Z.; Wang, B.; Xiang, J., & Liu, B. (2007). The Complete Mitochondrial Genomes of Two Common Shrimps (*Litopenaeus vannamei* and *Fenneropenaeus chinensis*) and their Phylogenomic Considerations. *Gene*. Vol.403, No.1-2, (November 2007), pp. 98–109, ISSN 0378-1119.

Sherwood, L.; Klandorf, H. & Yancey, P.H. (2005). *Animal Physiology*, Brooks/Cole, ISBN 978-0-534-55404-0, Velmont, California. USA.

Shin, D.S.; Didonato, M.; Barondeau, D.P.; Hura, G.L.; Hitomi, C.; Berglund, J.A.; Getzoff, E.D.; Cary, S.C. & Tainer, J.A. (2009). Superoxide Dismutase from the Eukaryotic Thermophile *Alvinella pompejana*: Structures, Stability, Mechanism, and Insights into Amyotrophic Lateral Sclerosis. *Journal of Molecular Biology*, Vol.385, No.5, (February 2009), pp. 1534-1555, ISSN 0022-2836.

Silvestre, F.; Dierick, J.F.; Dumont, V.; Dieu, M.; Raes, M. & Devos, P. (2006). Differential Protein Expression Profiles in Anterior Gills of *Eriocheir sinensis* During Acclimation to Cadmium. *Aquatic Toxicology,* Vol.76, No.1, (January 2006), pp. 46-58, ISSN 0166-445X.

Sokolova, I.M. (2004). Cadmium Effects on Mitochondrial Function are Enhanced by Elevated Temperatures in a Marine Poikilotherm, *Crassostrea virginica* Gmelin (Bivalvia: Ostreidae). *The Journal of Experimental Biology*, Vol.207, No.15, (July 2004), pp. 2639-2648, ISSN 0022-0949.

Sokolova, I.M. & Sokolov, E.P. (2005). Evolution of Mitochondrial Uncoupling Proteins: Novel Invertebrate UCP Homologues Suggest Early Evolutionary Divergence of the UCP Family. *FEBS Letters*, Vol. 579, No. (2): 313-317, ISSN 0014-5793.

Soldatov, A.A.; Andreenko, T.I.; Golovina, I.V. & Stolbov, A. (2010). Peculiarities of Organization of Tissue Metabolism in Molluscs with Different Tolerance to External Hypoxia. *Zhurnal evoliutsionnoi biokhimii i fiziologii*, Vol.46, No.4, (July-August 2010), pp. 284-90, ISSN 0044-4529.

Sommer, A. & Portner, H.O. (1999). Exposure of *Arenicola marina* to Extreme Temperatures: Adaptive Flexibility of a Boreal and Subpolar Subpopulation. *Marine Ecology Progress Series*, Vol.181, (May 1999), pp. 215-226, ISSN 0171-8630.

Soñanez-Organis, J.G.; Peregrino-Uriarte, A.B.; Gomez-Jimenez, S.; Lopez-Zavala, A.; Forman, H.J. & Yepiz-Plascencia, G. (2009). Molecular Characterization of Hypoxia Inducible Factor-1 (HIF-1) from the White Shrimp *Litopenaeus vannamei* and Tissue-Specific Expression under Hypoxia. *Comparative Biochemistry and Physiology Part C*, Vol.150, No.3, (September 2009), pp. 395-405, ISSN 1532-0456.

Staton, J.L.; Daehler, L.L. & Brown, W.M. (1997). Mitochondrial Gene Arrangement of the *Horseshoe* Crab *Limulus polyphemus L.*: Conservation of Major Features Among Arthropod Classes. *Molecular and Biological Evolution,* Vol.14, No.8, (August 1997), pp. 867-874, ISSN 0737-4038.

Steinauer, M.L; Nickol, B.B.; Broughton, R. & Orti, G. (2005). First Sequenced Mitochondrial Genome from the Phylum Acanthocephala (*Leptorhynchoides thecatus*) and its Phylogenetic Position within Metazoa. *Journal of Molecular Evolution,* Vol.60, No.6, (January 2005), pp. 706-15, ISSN 0022-2844.

St. John, J.C.; Jokhi, R.P. & Barrat, C.L.R. (2005). The Impact of Mitochondrial Genetics on Male Infertility. *International Journal of Andrology*, Vol.28, No.2, (April 2005), pp.65-73, ISSN 0105-6263.

Storey, K.B. (1993*). Molecular Mechanisms of Metabolic Arrest in Mollusks*. In*: Surviving Hypoxia: Mechanisms of Control and Adaptation* (eds. Hochachka, P.W., Lutz, P.L., Sick, T.J., Rosenthal, M., and Thillart, G. van den), pp. 253-269. CRC Press, Boca Raton.

Storz, P. (2006). Reactive Oxygen Species-Mediated Mitochondria-to-Nucleus Signaling: A Key to Aging and Radical-caused Diseases. *Science Signaling*, Vol.2006, No.332, (April 2006), pp. re3, ISSN 1937-9145.

Stuart, J.A. & Brown, M.F. (2006). Energy, Quiescence and the Cellular Basis of Animal Life Spans. *Comparative Biochemistry and Physiology Part A.* Vol.143, No.1, (January 2006), pp. 12–23, ISSN 1095-6433.

Suarez, R.K.; Staples, J.F.; Lighton, J.R. & Mathieu-Costello, O. (2000). Mitochondrial Function in Flying Honeybees (*Apis mellifera*): Respiratory Chain Enzymes and Electron Flow from Complex III to Oxygen. *The Journal of Experimental Biology*, Vol.203, (March 2000), pp. 905–911, ISSN 0022-0949.

Suga, K.; Mark-Welch, D.B.; Tanaka, Y.; Sakakura, Y. & Hagiwara, A. (2008). Two Circular Chromosomes of Unequal Copy Number Make Up the Mitochondrial Genome of the Rotifer *Brachionus plicatilis. Molecular Phylogenetics and Evolution*, Vol.25, No.6, (January 2008), pp. 1129-37, ISSN 1055-7903.

Talamillo, A.; Chisholm, A.A.; Garesse, R.; & Jacobs, H.T. (1998). Expression of the Nuclear Gene Encoding Mitochondrial ATP synthase Subunit Alpha in Early Development

of Drosophila and Sea Urchin. *Molecular Biology Reports*. Vol.25, No.2, (March 1998), pp. 87-94, ISSN 0301-4851.

Terrett, J.A.; Miles, S. & Thomas, R.H. (1996). Complete DNA Sequence of the Mitochondrial Genome of *Cepaea nemoralis* (Gastropoda: Pulmonata). *Journal of Molecular Evolution,* Vol.42, No.2, (February 1996), pp. 160-8, ISSN 0022-2844.

Toivonen, J.M.; O'Dell, K.M.C.; Petit, N.; Irvine, S.C.; Knight, G.K.; Lehtonen, M.; Longmuir, M.; Luoto, K.; Touraille, S.; Wang, Z.; Alziari, S.; Shah, Z.H. & Jacobs, H.T. (2001). Technical knockout, a Drosophila Model of Mitochondrial Deafness. *Genetics*, Vol.159, No.1, (September 2001), pp. 241–254, ISSN 0016-6731.

Tuena de Gomez-Poyou, M.; Perez-Hernandez, G. & Gomez-Poyou A. (1999). Synthesis and Hydrolysis of ATP and the Phosphate-ATP Exchange Reaction in Soluble Mitochondrial F_1 in the Presence of Dimethylsulfoxide, *European Journal of Biochemistry*, Vol.266, No.2, (December 1999), pp. 691-696, ISSN 0014-2956.

Turrens, J.F. (2003). Mitochondrial Formation of Reactive Oxygen Species. *The Journal of Physiology*, Vol.552, No.2, (October 2003), pp. 335-344, ISSN 0022-3751.

Uno, T.; Nakasuji, A.; Shimoda, M. & Aizono, Y. (2004). Expression of Cytochrome c Oxidase Subunit 1 Gene in the Brain at Early Stage in the Termination of Pupal Diapauses in the Sweet Potato Hornworm *Agrius convolvuli*. *Journal of Insect Physiology*, Vol.50, No.1, (January 2004), pp. 35-40, ISSN 0022-1910.

Van der Giezen, M. (2009). Eukaryotic Life Without Mitochondria?. *Comparative Biochemistry and Physiology Part A*, Vol.153, (June 2009), pp. S165–S167, ISSN 0300-9629.

Vendemiale, G.; Grattagliano, I.; Caraceni, P.; Caraccio, G.; Domenicali, M.; Dall'Agata, M.; Trevisani, F.; Guerrieri, F.; Bernardi, M. & Altomare, E. (2001). Mitochondrial Oxidative Injury and Energy Metabolism Alteration in Rat Fatty Liver: Effect of the Nutritional Status. *Hepatology,* Vol.33, No.4, (April 2011), pp. 808-815, ISSN 0270-9139.

Vishnudas, V. & Vigoreaux, J.O. (2006). Sustained High Power Performance Possible Strategies for Integrating Energy Supply and Demand in Flight Muscle, In: *Nature's Versatile Engine: Insect Flight Muscle Inside and Out,* J.O. Vigoreaux, (Ed.), 188-196, Springer, ISBN 978-0387257983, NY, USA.

Voigt, O.; Erpenbeck, D. & Worheide, G. (2008). A Fragmented Metazoan Organellar Genome: Two Mitochondrial Chromosomes of *Hydra magnipapillata*. *BMC Genomics,* Vol.9, (July 2008), pp. 350, ISSN 1471-2164.

Wang, B.; Li, F.; Dong, B.; Zhang, X.; Zhang, C. & Xiang, J. (2006). Discovery of the Genes in Response to White Spot Syndrome Virus (WSSV) Infection in *Fenneropenaeus chinensis* through cDNA Microarray. *Marine Biotechnology*, Vol.8, No.5, (September-October 2006), pp. 491-500, ISSN 1436-2228.

Wang, C. & Youle, R. (2009). The Role of Mitochondria in Apoptosis. *Annual Review of Genetics*, Vol.43, pp. 95-118, ISSN 0066-4197.

Wang, T.; Lefevre, S.; Thanh-Huong D.T.; van Cong N. & Bayley M. (2009). The Effects of Hypoxia on Growth and Digestion, *Fish Physiology*, Vol. 27, (February 2009), pp. 361-396, ISSN 0920-1742.

Watanabe, K. (2010). Unique Features of Animal Mitochondrial Translation Systems. The Non-Universal Genetic Code, Unusual Features of the Translational Apparatus and their Relevance to Human Mitochondrial Diseases. *Proceedings of the Japan Academy. Series B*, Vol.86, No.1, pp. 11-39, ISSN 0386-2208.

Wegener, G. (1996). Flying Insects: Model Systems in Exercise Physiology. *Experientia*, Vol.52, No.5, (May 1996), pp. 404-12, ISSN 0014-4754.

Wei, Y.H.; Lu, C.Y.; Lee, H.C.; Pang, C.Y. & Ma, Y.S. (1998). Oxidative Damage and Mutation to Mitochondrial DNA and Age-dependent Decline of Mitochondrial Respiratory Function. *Annals of the New York Academy of Sciences*, Vol.854, (November 1998), pp. 155-170, ISSN 0077-8923.

Wei, L.Z.; Zhang, X.M.; Li, J. & Huang, G.Q. (2008). Compensatory Growth of Chinese Shrimp, *Fenneropenaeus chinensis* Following Hypoxic Exposure. *Aquaculture International,* Vol.16, No.5, pp. 455-470, ISSN 0967-6120

Williams, T.; Chitnis, N.; & Bilimoria, S. (2009). Invertebrate Iridovirus Modulation of Apoptosis. *Virologica Sinica*, Vol.24, No.4, (August 2009), pp. 295-304, ISSN 1674-0769.

Wilson, D.F.; Rumsey, W.L.; Green, T.J. & Vanderkooi, J.M. (1988). The Oxygen Dependence of Mitochondrial Oxidative Phosphorylation Measured by a New Optical Method for Measuring Oxygen Concentration. *The Journal of Biological Chemistry.* Vol.263, No.6, (February 1988), pp. 2712-2718, ISSN 0021-9258.

Wittig, I.; Carrozzo, R.; Santorelli, F.M. & Schägger, H. (2006). Supercomplexes and Subcomplexes of Mitochondrial Oxidative Phosphorylation. *Biochimica et Biophysica Acta,* Vol. 1757, No.9-10, (September-October 2006), pp.1066-1072, ISSN 0006-3002.

Wittig, I. & Schägger, H. (2009). Supramolecular Organization of ATP synthase and Respiratory Chain in Mitochondrial Membranes. *Biochimica et Biophysica Acta*. Vol.1787, No.6, (June 2009), pp. 672-680, ISSN 0006-3002.

Wolstenholme, D.R.; Okimoto, R. & Macfarlane, J.L. (1994). Nucleotide Correlations that Suggest Tertiary Interactions in the TV-Replacement Loop-Containing Mitochondrial tRNAs of the Nematodes, *Caenorhabditis elegans* and *Ascaris suum*. *Nucleic Acids Research*, Vol.22, No.20, (October 1994), pp. 4300-6, ISSN 0305-1048.

Wu, R.S. (2002). Hypoxia: from Molecular Responses to Ecosystem Responses. *Marine Pollution Bulletin*, Vol.14, No.45, pp. 35-45, ISSN 0025-326X.

Xia, D.; Yu. C.A.; Kim, H.; Xia, J.Z.; Kachurin, A.M.; Zhang, L.; Yu, L. & Deisenhofer, J. (1997). Crystal Structure of the Cytochrome bc1 Complex from Bovine Heart Mitochondria. *Science*, Vol.277, No.5322, (July 1997), pp. 60-66, ISSN 0036-8075.

Yang, J.; Zhu, J. & Xu, W.H. (2010). Differential Expression Phosphorylation of COX Subunit 1 and COX Activity During Diapause Phase in the Cotton Bollworm *Helicoverpa armigera*. *Journal of Insect Physiology*, Vol.56, No.12, (December 2010), pp. 1992-1998, ISSN 0022-1910.

Yang, W. & Hekimi, S. (2010). A Mitochondrial Superoxide Signal Triggers increased Longevity in *Caenorhabditis elegans*. *PLos Biology*, Vol. 8, No. 12, (December 2010), pp. e1000556, ISSN 1544-9173.

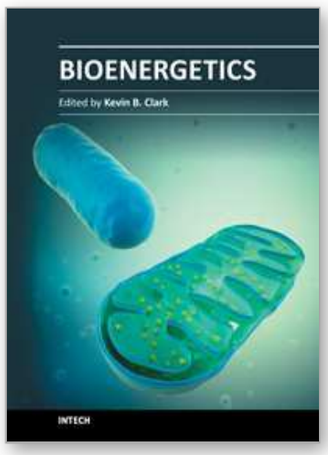
Yasuda, N.; Hamaguchi, M.; Sasaki, M.; Nagai, S.; Saba, M. & Nadaoka, K. (2006). Complete Mitochondrial Genome Sequences for Crown-of-thorns Starfish *Acanthaster planci* and *Acanthaster brevispinus*. *BMC Genomics*. Vol.7, (January 2006), pp. 17, ISSN 1471-2164.

Yokobori, S.; Ueda, T.; Feldmaier-Fuchs, G.; Pääbo, S.; Ueshima, R.; Kondow, A.; Nishikawa, K. & Watanabe, K. (1999). Complete DNA Sequence of the Mitochondrial Genome of the Ascidian *Halocynthia roretzi* (Chordata, Urochordata). *Genetics*, Vol.153, No.4, (December 1999), pp. 1851-1862, ISSN 0016-6731.

Yu, X.X.; Mao, W.; Zhong, A.; Schow, P.; Brush, J.; Sherwood, S.W.; Adams, S.H. & Pan, G. (2000). Characterization of Novel UCP5/BMCP1 isoforms and Differential Regulation of UCP4 and UCP5 Expression through Dietary or Temperature Manipulation. *The FASEB Journal*, Vol. 14, No. 11. (August 2000), pp. 1611-1618, ISSN 892-6638.

Yu, H. & Li, Q. (2011). Complete Mitochondrial DNA Sequence of *Crassostrea nippona*: Comparative and Phylogenomic Studies on Seven Commercial *Crassostrea* species. *Molecular Biology Reports*, (May 2011), ISSN 1573-4978.

Zickermann, V.; Dröse, S.; Tocilescu, M.A.; Zwicker, K.; Kerscher, S. & Brandt, U. (2008). Challenges in Elucidating Structure and Mechanism of Proton Pumping NADH: Ubiquinone Oxidoreductase (Complex I). *Journal of Bioenergetics and Biomembranes*. Vol.40, No.5, (October 2008), pp. 475-483, ISSN 0145-479X.



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Cellular life depends upon energy storage, transformation, utilization, and exchange in order to optimally function and to stay-off death. The over 200-year-old study of how cells transform biological fuels into usable energy, a process broadly known as bioenergetics, has produced celebrated traditions in explaining origins of life, metabolism, ecological adaptation, homeostasis, biosynthesis, aging, disease, and numerous other life processes. InTech's edited volume, Bioenergetics, brings together some of these traditions for readers through a collection of chapters written by international authorities. Novice and expert will find this book bridges scientific revolutions in organismic biology, membrane physiology, and molecular biology to advance the discipline of bioenergetics toward solving contemporary and future problems in metabolic diseases, life transitions and longevity, and performance optimization.

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Unit 405, Office Block, Hotel Equatorial Shanghai
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