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## Alternative Therapy of Cancer

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Tumors are the result of localized, unregulated, cell growth. For a tumor to become malignant, cells must begin to metastasize (move), and invade other tissues. The original tumor is called a primary tumor, and all the cells derive from single aberrant cell. As tumors metastasize the new colonies, or foci, are referred to as secondary tumors or metastatic centers. Each center will arise from a different founder cell but all will derive from the single founder cell of the primary tumor.

Cell signaling is part of a complex system (Reuven and Havlin, 2010) of communication that governs basic cellular activities and coordinates cell actions. The ability of cells to perceive and correctly respond to their microenvironment is the basis of development, tissue repair, and immunity as well as normal tissue homeostasis. Errors in cellular information processing are responsible for diseases such as cancer, autoimmunity, and diabetes. By understanding cell signaling, diseases may be treated effectively and, theoretically, artificial tissues may be created.

In normal cells, growth, division, and differentiation are highly regulated processes. Some signaling molecules (growth factors) promote cell division. Other signaling molecules cause cells to stop growing. Many signaling molecules, including growth factors and growth inhibitors, bind to receptors on the surface of the cell. In many cases, these receptors must interact with one another, or dimerize, before they can become fully activated. Once they are activated, receptors activate relay teams of proteins inside the cell (signaling pathways) (Dinasarapu et al., 2011).

Activated signaling pathways carry messages from the receptor to the inside of the cell and sometimes all the way to the DNA in the nucleus. Activation of these signaling pathways is often carried out by the transfer of chemicals, called phosphates, from one member of the relay team to the next. This process is known as phosphorylation. Receptors and other proteins that perform phosphorylation are called kinases (Alberts et al., 2002; Dinasarapu et al., 2011). The messages carried by the activated signaling pathways lead to the accumulation and activation of certain proteins that either promote or inhibit cell growth and division. The rate of cell growth and division depends on the balance of these two types of signals.

Cancer is thought to be mutations in genes for signal transduction components, the first indications of this came from studies of DNA tumor viruses that infected non-human vertebrates. It was established that particular genes in the genomes of these viruses (termed oncogenes) were responsible for tumor promotion. With time and the convergence of cellular and viral oncology, it was realized that oncogenes were the mutant counterparts of normal cellular genes. The cellular genes are called proto-oncogenes. Many of the cellular counterparts of oncogenes have now been identified (and cloned), and it is clear that most are components of some form of signal transduction pathway. The signaling systems are used by cells to make decisions like grow/don't grow, move/don't move or change patterns of gene expression. Many of these cellular components are the same kinds of factors to be the driving forces behind the fundamental mechanisms of developmental decision making.

Little wonder then that the mechanisms that control development and go out of control in cancer seem so intimately related. Characteristically, oncogenes derange growth regulation by hyperactivating growth stimulatory signals; thus normal growth control is overridden. Because the mutations generally produce an over stimulation of a positive signal, only one mutant copy of the gene is required to provide the phenotype. Consistent with this, most oncogenes are dominant mutations.

There is, however, another way to get over stimulation of a positive signal. That is to have a recessive, lose of function, mutation in a negative regulator of the signal. This is the basis for another group of genes found to be mutant in many cancers; called tumor suppressor genes or anti-oncogenes (neither name is completely satisfying). One of the clearest indications of the existence of such genes came from experiments in which tumor-producing and non-tumor-producing cells were fused together. With rare exceptions (which turned out to be important) the fused cells were non-tumorigenic (suppressing tumor formation).

### **Cancer production**

*One of the fundamental traits of cancer cells is their ability to proliferate without a controlled signaling input. They achieve this in a number of ways:* Increasing growth factor production, Stimulating normal cells in the microenvironment to provide cancer cells with growth factors, increasing the number of receptors on the cell surface, structurally altering receptors to facilitate cancer cell signaling and activating proteins in the downstream signaling pathway. Recent studies also highlight the ability of cancer cells to disrupt negative feedback loops that constitute a safety mechanism to dampen a signaling pathway whenever a mitogenic signal is hyperactivated. One key example of this is the RAS oncoprotein. Oncogenic activity of RAS is not the result of overactive RAS signaling but rather the disruption of normal negative feedback mechanisms operated by the oncogenic GTPase. Other examples of this process include loss-of-function mutations in phosphatase and tensin homolog (PTEN), which amplify phosphatidylinositol 3-kinase (PI3K) signaling.

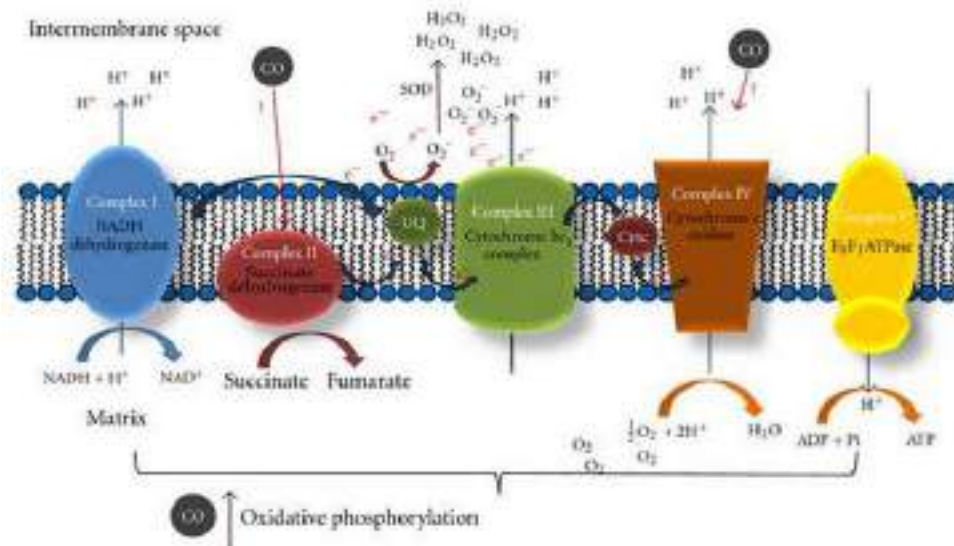
*Tissue invasion and metastasis* are integral components in how tumor cells escape from the primary site and disseminate into distant organs. The process of tissue invasion and metastasis is not well understood, but, in general, it involves changes in the way cells attach to other cells and to the extracellular matrix (Trail and Bianchi, 1999; Wu and Senter, 2005).

*Immune surveillance* is an essential cellular process that proactively prevents tumor formation in the human body. Preclinical studies have suggested that an active immune system continuously recognizes and eliminates the vast majority of cancer cells before they establish themselves and form a tumor mass (Trail and Bianchi, 1999; Wu and Senter, 2005).

*In tumor cells, the process of angiogenesis*, or the formation of new blood vessels, is critical for sustained tumor growth and metastasis. Tumor angiogenesis is a multistep process and involves signaling input from several pro-angiogenic growth factors (Trail and Bianchi, 1999; Wu and Senter, 2005; Chari, 2008).

### **Cancer is a redox disease?**

Every living cell needs energy. The source of energy that is used by a cell varies depending on for example the cell type and its environment. In every cell the energy needs to be converted in order to be accessible for energy-requiring processes such as growth, organization, transport and reproduction. Metabolism is a set of chemical reactions involved in the uptake, conversion, digestion and excretion of energy-containing nutrients.



*Fig. 65: Every living cell needs energy. The source of energy that is used by a cell varies depending on for example the cell type and its environment. The key players of metabolism, catalyzing the chemical reactions, are enzymes. Mitochondria contain the enzyme complexes of metabolic processes, most of the adenosine triphosphate (ATP), which is the molecule essential for many energy-requiring reactions in the cell, is generated in mitochondria. Mitochondria also contain their own genetic material; mitochondrial DNA (mtDNA).*

There is growing realization that cancer is not primarily a genetic disease, but an epigenetic response to chronic stress. Cancer cells, however, depend heavily on glycolysis to obtain energy, even though plenty of oxygen is present. This phenomenon – aerobic glycolysis subsequently known as the Warburg effect - prompted Warburg to propose that mitochondrial dysfunction was the primary cause of cancer. Aerobic glycolysis is a robust hallmark of most tumours; it involves a high uptake of glucose with lactate production in the presence of oxygen, lactate being the by-product of pyruvate, even in those cancer cells that appear to have working mitochondria . The reason seems to be that cancer cells need glycolysis to generate carbon skeletons for the synthesis of proteins and nucleic acids to support rapid cell proliferation ; and blocking glycolysis does appear to inhibit cancer cells (though it would also affect normal cells). Reduction and oxidation always go together, hence ‘redox’ reactions. Redox reactions are the heart of energy transduction in living organisms. Electrons move according to the *reduction potential* (also referred to as reduction-oxidation potential or redox potential), the affinity of a substance for electrons. The redox potential for each substance is

compared to that of hydrogen, which is set arbitrarily to zero at standard conditions of 25 °C, 1 atmosphere, and 1 M concentration (ISIS, 2012).

ROS play multiple roles in the hallmarks of cancers. ROS play a role in ligand-independent RTK transactivation, decreased RTK activation threshold (Storz, 2005, involved in p53 activation, loss of contact inhibition, and loss of anchorage dependence (Pani et al., 2010). ROS play a role in Met overexpression, matrix metalloproteinase secretion, in vadopodia formation, and plasticity in cell motility, EMT (Svineng et al., 2008). ROS are involved in expression of telomerase (Pani et al., 2010). ROS are involved in increasing the rates of mutation, increasing sensibility to mutagenic agents, and compromising the surveillance systems (Hanahan and Weinberg, 2011).

### **Energy metabolism of cancer cells**

Cancer cells, to a much higher extent than normal cells, rely on glycolysis for production of ATP (Gogvadze et al., 2010) This phenomenon is called “aerobic glycolysis”, or the Warburg effect, and has been known for over 50 years to be a common feature of tumor cells. The mechanisms of reprogramming are complex, involving activation or deactivation of a large number of genes (Kroemer. and Pouyssegur, 2008)

The amino-acid substitutions found in colon cancer resulted in a lowered Cyt<sub>c</sub>O activity as compared to the wild-type enzyme. A lowered Cyt<sub>c</sub>O catalytic activity could lead to a decreased rate of electron flux through the entire respiratory chain and thus insufficient amounts of ATP being produced. In addition, with the Tyr33His Cyt<sub>c</sub>O the oxygen reduction was uncoupled from proton pumping. A decreased synthesis of ATP through oxidative phosphorylation might however not be as devastating for a cancer cell as for a normal cell, due to the metabolic shift occurring in tumors. In fact, a defective respiratory-chain activity could contribute to initiating the metabolic reprogramming that occurs in cancer cells.

Amino-acid substitutions in Cyt<sub>c</sub>O have been found for example in prostate cancer, pancreatic cancer and ovarian cancer. In addition, substitutions in Cyt<sub>c</sub>O have been reported in normal colonic crypt stem cells in colon cancer patients (Petros et al., 2005; Pye et al., 2006).

Several studies have shown that chemical inhibition of Cyt<sub>c</sub>O activity could in fact lead to increased ROS formation from other respiratory-chain complexes. An increased ROS production due to Cyt<sub>c</sub>O inhibition by azide has been observed in both mammalian cells and submitochondrial particles (Dawson et al., 1993; Jacobson et al., 2005; Prabhakaran et al., 2002). In these cases the suggested mechanism is that the inhibition of Cyt<sub>c</sub>O causes an increased leak of electrons, and hence ROS formation.

### **Mechanisms of Cell genotoxic stress control**

The ability of cells to maintain genomic integrity is vital for cell survival and proliferation. Lack of fidelity in DNA replication and maintenance can result in deleterious mutations leading to cancer. Surveillance control mechanisms that check to ensure proper completion of early events and cellular integrity before initiation of subsequent events in cell cycle progression are referred to as cell cycle checkpoints and can generate a transient delay that provides the cell more time to repair damage

before progressing to the next phase of the cycle. A variety of cellular responses are elicited that function in checkpoint signaling to inhibit cyclin/Cdk activities. These responses include the p53-dependent and p53-independent induction of Cdk inhibitors and the p53-independent inhibitory phosphorylation of Cdk molecules themselves. Several human heritable cancer-prone syndromes known to alter DNA stability have been found to have defects in checkpoint surveillance pathways. Exposures to several common sources of genotoxic stress, including oxidative stress, ionizing radiation, UV radiation, and the genotoxic compound benzo[a]pyrene, elicit cell cycle checkpoint responses that show both similarities and differences in their molecular signaling [Shackelford et al., 1999; Doherty et al., 2003].

However, there is evidence that the cell's loss of electron-donor properties is followed by its transfer into such a phase of individual development (ontogenesis) whose histological characteristics are similar to those of the phenomenon of functional-morphological differentiation associated with the loss of normal proliferation activity and subsequent aging or malignization.

### **Suggested novel therapy**

#### **Electrochemically activated water (ECA-water)**

Water as a pure chemical substance or as a solvent of aqua-mineral media of mineralization no higher than  $\approx 5$  g/l subjected to unipolar electrochemical treatment, metastable, possessing anomalous reactional and catalytic activity and relaxation electron-unbalanced (electron-donor or electron-acceptor) qualities

“Alkaline (cathodic, “live”) water stimulates wound healing, relieves pain of inflammatory processes and burns. It certainly augments cell regeneration and development. Neither effect could be achieved by simply acidifying or alkalizing source water: it follows that it is the ability of an activated system” . Super-active particles emerging during electrochemical synthesis due to their metastability are subject to spontaneous decomposition in the process of solutions' relaxation. Consequently, the ORP values of electrochemically treated diluted aqua-mineral media also relax. The nature of anomalous reaction ability and catalytic activity of anolyte and catholyte produced from low mineralization water is associated with the unique assemblage of highly-active metastable particles formed by electrolysis, and with specific physical conditions arising in an electrochemical reactor.

In fact, “live water” is the only antioxidant which can be introduced into a human body in doses of about several hundred milliliters. Drinking catholyte is very likely to create general electron-donor background in CBV and water sector due to physical dilution of electron-donor carrier. Similar effect is achieved when antioxidants are directly or indirectly introduced into tissue media of arthropoda (cricket's hemolymph) or into tissue mass of small mammalia. At that, tissue media ORP markedly lowers, and their radioresistance rises. ORP decrease is also found to stimulate better radioresistance of living body tissues irrespective of the way. Exo- and endogenous antioxidants have similar antiactinic activity. Therefore, electrochemical technologies can be regarded as available, safe and non-reagent means of monitoring the systems of body antioxidant and antiactinic protection.

In biological substrates approximate  $\varphi_s$  range from (-250) to 1000 mV, CSE is most common. Spread in biological media pH values usually does not exceed 6.0–8.0. Intracellular acidosis accompanied by pH shift to values lower than 6.0 (for instance, in acute myocardial ischemia) is associated with necrobiosis formation. Liver cells' pH decrease to values lower than 7.0 results in essential functional hepatic disorders. Blood values over 7.6 are life threatening (36). Thus, pH-dependent ORP variations of biological media in conformity with  $\varphi_{st}^{\bullet}/\text{pH}$  regression (see formula (6)) may reach up to 100 mV. (Not counting committant changes of the  $[\text{Ox}]/[\text{Red}]$  ratio.

Permissible ORP variations of internal body media are explored insufficiently. According to G.V. Sumarukov (37) small laboratory animals (mice, rats) survive after intraperitoneal introduction of radioprotectors associated with ORP regression in the tissues of brain, liver, kidneys, muscles, bone marrow of about 100–200 mV.

In acute ischemia the ORP of mammalian brain tissue increases by 60–80 mV. On the whole, judging by the data presented one may suggest that microecological conditions of the body internal medium with  $\text{pH} < 6.0$  and  $\text{ORP} > 400$  mV, CSE, are incompatible with normal cell life activity. Formal upper physiological limit of tissue ORP in the range of 6.8–8.0 is not established. The lowest permissible physiological limits of ORP in the body are also unclear. In protein-cellular media of mammals at  $\text{pH} < 6.0$  and  $\text{pH} > 8.0$  gross functional impairment grows. At pH range of 3.0–4.0 most dissolved proteins undergo irreversible coagulation. When pH values of protein media shift to the range of 9.0–10.0 there occurs protein molecules aggregation, which is mostly of irreversible nature (40). The above stated facts are definitely applied only to the situations when acidulation or alkalization of protein solutions takes place in the absence of ECA methods, i.e. with the help of routine acid and base solutions. But there are all reasons to expect anolyte and catholyte with a pH shift (and, consequently, an ORP one) to possess abiotic properties in the area of extremal values.

In 1975, Yu.P. Kozlov drew forth numerous data on the way of action of different biooxidants, in particular, free radicals in the body tissues and biological fluids. Augmented processes of free radical oxidation on the tissue level are followed by accumulation of lipoperoxides or the products of peroxide oxidation of lipids (POL) in cell membranes, organoids, particularly mitochondria, resulting in a greater rate of oxygen utilization and dissociated oxidative phosphorylation. Enhanced oxygen consumption by the tissues also intensifies POL products formation, which is associated with certain pathophysiological consequences. At that, enhanced oxygen utilization may become inadequate to oxygen delivery to the tissues with blood.

On the background of peroxide oxidizing activation, energetic efficiency of the body oxygen utilization decreases due to the fact that part of oxygen is spent on direct (non-enzymatic) interaction with substrates of low energetic value. Lipoperoxides possess high cytoplasmic toxicity, irreversibly denature enzymatic proteins, easily cause enzymes' polymerization, produce destructive action on the main enzymes of glycolysis, tricarboxylic cycle, as well as on the basic macroergic compound of the body – ATP. Severe depletion of tissue respiration in this case is inevitable.

By their nature free radicals and lipoperoxides are the agents of electron-acceptor action. Anolyte is an electron-acceptor medium with anomalously enhanced electron-acceptor properties. But it doesn't automatically follow that anolyte upsets tissue respiration in all cases.

Common oxygen is known to be one of the strongest biooxidants, but its toxic action manifests itself only as a response to overdosage. Similarly, anolyte action on a biological substrate should be dual. Anolyte with relatively weak or moderate electron-donor characteristics can stimulate biological oxidation, in particular, oxidative phosphorylation, thus increasing intensity of tissue respiration. Anolyte with increased concentration of strong oxidants, including peroxide compounds, and with pathologically high ORP values is to cause cytotoxic and antimetabolic effect. In this case, anolyte's action will be accompanied with suppressed tissue respiration, elevated anaerobic energogenesis, accumulated underoxidized slags, decreased BE, ABB shift towards metabolic acidosis, tissue microcirculation disturbances, forced pulmonary respiration function. In the conditions of metabolic acidosis, circulatory tissue hypoxia, including probable metabolic disturbances, demonstrates the trend to enhanced electron-donor background of the body's internal medium, and in this manner makes up for the trend to enhancing electron-acceptor background, associated with pH value reduction, and also acts as one of natural mechanisms of antioxidant defense. Catholyte elevating the electron-donor background of fluid biological media similarly manifests itself as a factor of antioxidant defense. However, under certain conditions of electrochemical treatment catholyte may contain free radicals possessing cytotoxic and antimetabolic action. Excessive depression of the ORP of biological media during catholyte overdosage is capable of imposing a thermodynamic ban on normal processes of biological oxidation. That is why formal division of ECA-solutions into "live" and "dead" water depending on the type of electrochemical treatment (anodic or cathodic) is very relative. A likely pathogenesis scheme of biochemical and physiological disturbances caused by electron-acceptor factors, including strong oxidants of ECA-media and ORP anomalous deviations

Consequently, it is right to assume that there may be optimal, physiologically beneficial doses of ECA-solutions of A, AN, C and other types. A diagram of sanogenetic action of therapeutic doses of anolyte and other electron-acceptor factors is presented in Fig. 63.

Therapeutic doses of anolyte and other electron-acceptor media, when ingested enterally, are supposed to disinfect gastro-intestinal tract, promote terminal oxidation of under-oxidized toxic products of metabolism, thus performing oxidative detoxification, removing thermodynamic restrictions from enzymatic oxidation processes, and stimulate energogenesis and general catabolic processes.

Detoxification mechanism of the internal medium under the action of anolyte can be seen from the example of oxidative hydroxylation of hydrophobic organic toxins taking place with the help of hypochlorite usually present in anolyte's composition. Oxidative phosphorylation reaction goes on according to the following formula:  $RN + NaClO \rightarrow ROH + NaCl$ , where R stands for organic radical, RH is organic hydrophobic compound, ROH – oxidative hydroxylation product. ROH derivatives are low toxic, hydrophilic and can be easily removed thanks to physiological excretion.



Fig.66: **A diagram of synergistic action of electron-acceptor factors in the internal body medium.**

Pathogenesis of peroxide homeostasis disturbances in conditions of antioxidant factor deficiency in the body can be described in the following way (49). Introduction of only one sulfur-containing exogenous antioxidant (cystamine) into the internal medium in the absence of ascorbate and tocopherol is inefficient, since failure of the system of free-radical oxidation inhibition occurs **if at least one component of anti-radical group** is missing. Peroxidase used in cases when the diet lacks antioxidants, spends glutathione and ascorbate thus destroying peroxides. These conditions induce failure of the main anti-radical group of inhibition system, accelerating development of free-radical oxidation, in spite of augmented peroxide breakdown.

It can be added that balance of anti-radical chain elements seems to be a necessary but insufficient prerequisite for efficient suppression of free radicals' activity, since electron transfer in accordance with the system: enzymatic oxidation products  $\rightarrow$  NADP-H  $\rightarrow$  glutathione  $\rightarrow$  ascorbate  $\rightarrow$  tocopherol, depends on the ORP value of fluid media, among which there is an anti-radical defense system. Catholyte is **the only** means of non-reagent shift of biological fluids ORP towards electron-donor values. Increased tissue reductive potential ( $\Delta\text{ORP} < 0$ ) stimulates the transfer of two hydrogen atoms from the substrate to NADP. At that, NADP is reduced: a proton and an electron add to a nicotine-amide radical, and another electron adds to its N-atom, which due to that loses its charge. A proton corresponding to this electron remains in the medium and raises its  $[\text{H}^+]$  content. .

NADP reduction is a two-electron reaction and such reactions ( $n=2$ ) ORP shift of only  $(-0.029\text{V})$  corresponds to thermodynamic conditions, favorable for a clear prevalence of a reduced NADP-H form over an oxidized form of  $\text{NADP}^+$  ( $[\text{Red}]/[\text{Ox}] = 90:10$ ). Thus, ORP must exert a strong influence on the dynamics of electron-proton transport along the whole chain of anti-radical (anti-oxidant) biochemical defense.

#### **Hypothetical mechanisms of ECA-solutions' action on a cellular level.**

Action of ECA-solutions on cellular objects seems to be carried out in several conventional ways. Stable and metastable products of electrochemical synthesis directly affect lipid membranes, cell organoids and intracellular molecular complexes and chemical compounds. Oxidizing and reducing

agents of ECA-solutions alter the ORP of peri- and intracellular media, thus regulating the activity of endogenous biooxidants and bioantioxidants. Shifts of ORP gradient on biological membranes affect transfer of substances in the cell due to electroosmosis. Penetration of structurally altered water inside the cell activates aqueous media of cytoplasm and speeds up biochemical reactions taking place there.

Electronic equilibrium of cellular membranes is determined by the ratio of unsaturated and saturated fatty acids in them. C=C type diene bonds of unsaturated fatty acids' molecules possess electron-donor properties. Therefore, depending on the level of saturation or nonsaturation of external membrane lipids a cell may be to a greater or lesser extent an electron-donor object relative to intercellular fluid.

Electron-donor properties of a living cell are likely to correlate with its negative electric charge. Electrostatic charge of a typical cell of a mammal is  $(-60)$  mV (52). Electron-donor characteristics of lipid membranes are local, since diene bonds are fixed on the membranes' surface. In solutions, coming into direct contact with a biological membrane, electron-balanced properties not necessarily coincide with electron equilibrium of this membrane. This fact is illustrated by measuring the ORP of the some cell suspensions in model physiological media and in cell-free filtrates of these media.

Strong oxidants, among them electron-acceptor anolyte factors, cause cell membranes' damage, which, in its turn, negatively affects electron-donor properties of the cell. Electron-acceptor action of anodically activated solutions on bio-membranes is universal, since anolyte contains a variety of over-oxidized chemical forms, dissolved in a medium with a pathologically high ORP value. Because of that, acids and peroxides being a part of anolyte react with a cell object on the background of enhancing electron-donor qualities of biological fluids, which are a basis of biological substrate of peri- and intracellular system.

Anolyte is a complex of stable and metastable strong oxidants in an aqueous medium of super-high electron-acceptor activity, capable of quick propagation through biological barriers and passing of its electron-acceptor abilities via amorphous substrates. That creates prerequisites for a totally penetrative oxidation effect similar to that of general irradiation radiolysis. Therefore, anolyte (oxidant) and radiation load on the body or particular tissue systems are to have a number of common pathophysiological or therapeutic effects.

There is evidence that the cell's loss of electron-donor properties is followed by its transfer into such a phase of individual development (ontogenesis) whose histological characteristics are similar to those of the phenomenon of functional-morphological differentiation associated with the loss of normal proliferation activity and subsequent aging or malignization.

Irradiation of the body with ionizing radiation or growth of a malignant tumor is followed by elimination of free-radical oxidation products into blood and different internal media of the body, as well as by a lowered anti-inflammatory lipid activity. In the tissues of animals with tumors (in the liver, omentum, brain) lipid peroxide concentration increases as the tumor grows. However, in the tumor itself lipid peroxide content is reduced in comparison with normal tissues.

### **Anolyte kills cancer cells**

Strong oxidants, among them electron-acceptor anolyte factors, cause cell membranes' damage, which, in its turn, negatively affects electron-donor properties of the cell. Electron-acceptor action of anodically activated solutions on bio-membranes is universal, since anolyte contains a variety of over-oxidized chemical forms, dissolved in a medium with a pathologically high ORP value. Because of that, acids and peroxides being a part of anolyte react with a cell object on the background of enhancing electron-donor qualities of biological fluids, which are a basis of biological substrate of peri- and intracellular system.

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### **Catholyte augments cell regeneration and development**

"Alkaline (cathodic, "live") water certainly augments cell regeneration and development.

Oxidative phosphorylation reaction goes on according to the following formula:  $RN + NaClO \rightarrow ROH + NaCl$ , where R stands for organic radical, RH is organic hydrophobic compound, ROH – oxidative hydroxylation product. ROH derivatives are low toxic, hydrophilic and can be easily removed thanks to physiological excretion.

It can be added that balance of anti-radical chain elements seems to be a necessary but insufficient prerequisite for efficient suppression of free radicals' activity, since electron transfer in accordance with the system: enzymatic oxidation products  $\rightarrow$  NADP-H  $\rightarrow$  glutathione  $\rightarrow$  ascorbate  $\rightarrow$  tocopherol, depends on the ORP value of fluid media, among which there is an anti-radical defense system. Catholyte is the only means of non-reagent shift of biological fluids ORP towards electron-donor values. Increased tissue reductive potential ( $\Delta ORP < 0$ ) stimulates the transfer of two hydrogen atoms from the substrate to NADP. At that, NADP is reduced: a proton and an electron add to a nicotine-amide radical, and another electron adds to its N-atom, which due to that loses its charge. A proton corresponding to this electron remains in the medium and raises its  $[H^+]$  content.

According to the findings of studying laboratory and agricultural animals, receiving catholyte for drinking, the following conclusions can be made. Catholyte of drinking water or aqua-saline solutions with pH of about 9.0–9.5; ORP about  $(-400 \pm 50)$  mV, CSE at its ingestion at a volume equivalent to  $10 \pm 5\%$  of daily intake of drinking water produces the following effects on the organism of mammals and birds (Prilutsky and Bakhir, 1997): General invigorating action - Increases resistance of the body to ionizing irradiation and Elevates activity of tissue respiration enzymes.

There was an attempt of treating cancer patient dogs (Leukemia and Prostate) with the help of ECA-solutions. It started by i/v injection of one ml of anolyte per 10 kg live body weight daily for 2 weeks. At the same time treatment implied indication of shock doses of anolyte (450 ml per day) during 3 days followed by drinking catholyte doses of 300 ml daily during 5 days. Similar course with slight dosage alterations was repeated after 3 and 20 day intervals. The attempts were revealed 100 % curing success (Kaoud and Sobeh, 2015).

### **Electrically Reduced Water (ERW) (Anti-cancer effects)**

ERW causes telomere shortening in cancer cells (Shirahata et al., 1999). It suppresses tumor angiogenesis by scavenging intracellular ROS and suppressing the gene expression and secretion of vascular endothelial growth factor (Ye et al., 2008). ERW suppresses the growth of cancer cells and microorganisms (Hamasaki et al., 2005; Komatsu et al., 2001) and induces apoptosis together with glutathione in human leukemia HL60 cells (Tsai et al., 2009). ERW induces differentiation of K562 cells to megakaryocytes (Komatsu et al., 2003), and when supplemented with Pt nanoparticles, it strongly suppresses the two step transformation of NIH3T3 cells by a carcinogen (Nishikawa et al., 2005).

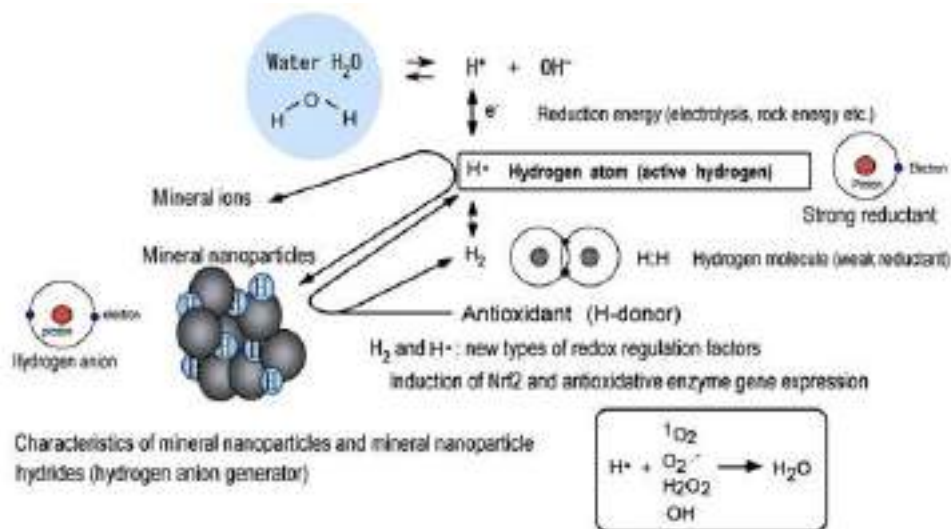


Fig. 66: ERW, water is reduced by electric energy, rock energy and other energy to produce active hydrogen (H atom) and mineral nanoparticles. H atoms produce hydrogen molecules, which are weak reductants, but can function as H-donors. Mineral nanoparticles sustain reduction energy, because they gradually dissociate to mineral ions, releasing electrons. Mineral nanoparticles directly scavenge O<sub>2</sub>, .OH and H<sub>2</sub>O<sub>2</sub> by catalysis mechanisms (:Shirahata et al., 2012).

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