From the Global to the Local

Possible Pathways for the Transduction of Indo-Sino-Tibetan Cognitive-Behavioral Practices into Site-Specific, Tissue-Regenerative Effects

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While skepticism regarding the possibilities for a productive meeting (metaphorically or actual) between Western medicine and biology and older healing and health practices of traditional cultures may be prevalent, there are many theoretical points of meeting and much experimental data to suggest that cognitive-behavioral practices (C-Bp) of the latter may induce testable and reproducible phenomena for the former. Such modulation or modification of tissue regeneration by C-Bp presumably must work through systemic signaling of some kind. Several possible mechanisms for such signaling are recognized and will be reviewed here: humoral, neurological, cell trafficking, and bioelectromagnetic/energy mediated. Nonetheless, while cultures and techniques may be varied, human bodies are more alike than dissimilar. We indicate that great profit may be had for all participating cultures in establishing a common language, shared criteria for designing experiments and interpreting data, and cooperative goals for the promotion of tissue integrity and regeneration.

Key words: **meditation; yoga; *pranayama*; acupuncture; regeneration; stem cells; innervation; melatonin; bioelectromagnetic**

The modulation or modification of tissue regeneration by cognitive-behavioral practices (C-Bp) presumably must work through systemic signaling of some kind. Several possible mechanisms for such signaling are recognized: humoral, neurological, cell trafficking, and bioelectromagnetic/energy mediated (Fig. 1).

Even a few short years ago, attempts to discern these various pathways in order to link the aspects of the global system of the body to site-specific regeneration, might have seemed impossible. The apparent inability to do so was, in part, tied to overly simplistic concepts of how and where regeneration might take place in the adult human. For example, taking the "hot topic" of stem cells, until recently, our knowledge of these cells was quite limited. Typically, organs with rapid cell turnover—bone marrow, skin, gastrointestinal tract, and reproductive organs (ovary/testis) which maintained the germline—were recognized as having stem cells; organs that had little obvious turnover, such as heart, brain, and liver, were considered unlikely to have them. As for the other organs, there was little certainty in either direction.

That was then. Now, less than a decade later, we know that virtually every tissue has a stem

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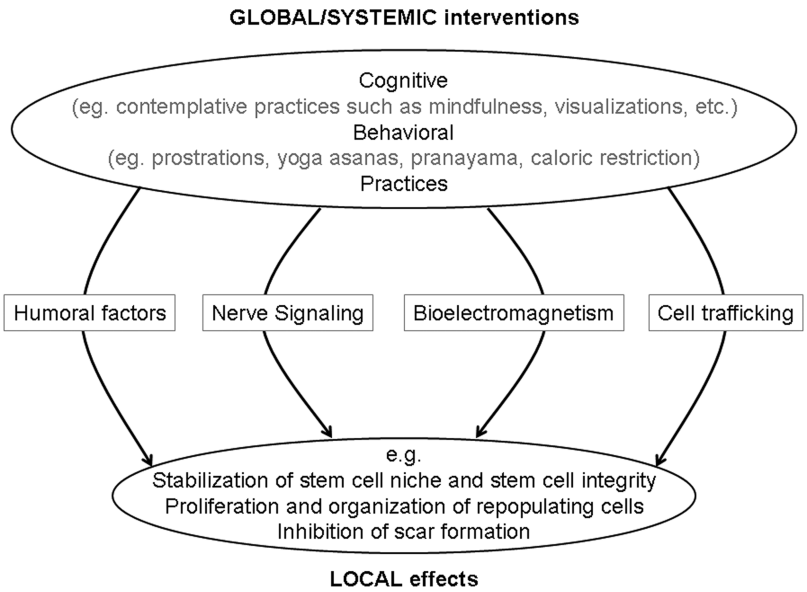

FIGURE 1. Pathways of transduction of cognitive-behavioral practices to local, site-specific tissue regeneration.

or at least progenitor cell component and that these may be situated in one or several locations within each organ as well as outside the organ. Indeed, it even seems apparent that cells may be trafficking between organs, between very different tissue types, to participate in repair.

For the purposes of this panel discussion, "regeneration," per se, will be mostly focused on a tissue level repair response following tissue injury. Clearly, dividing lines between "longevity," "protection," "optimization," and a possible renewal of "youthfulness" (also topics in this conference), and regeneration, are not easily drawn; these are all interrelated phenomena forming a web of simultaneous effects, not a hierarchical list of stepwise responses. Also, such a definition of regeneration as tissue repair is a meeting point of systemic processes on levels of scale above and cellular, molecular, and electromagnetic at levels of scale below.

So, this panel will seek to demonstrate two separate aspects of the question of how regeneration may be influenced by systemic C-Bp. The first is to define ways in which communication from a global effect can transmit to specific sites to create local effects. The second is to demonstrate that regenerative processes at those sites may be considerably more intricate, rich, and varied than was imagined in the last century (or, in some instances, even in the last year). This last point is important in inter-cultural dialogue of this kind, in that while Western practitioners of the biological sciences rightly take pride in how much we've learned, it remains abundantly clear from these newest biological frontiers that we know, in fact, very little, still, and that many surprises are likely to await us.

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As stated, an important aspect of C-Bp is that they are usually working on an apparent global level of the body as a whole. While phenomena of "aging" and "longevity" discussed by other panels are also global, regeneration is generally conceived of as local: this limb or that organ or this tissue needs repair after injury. To be sure there are medical practices, such as acupuncture, which appear in some respects to be global, but may in fact be local if the concept of "organ" or "tissue" is defined less rigidly than it is by Western gross anatomy. But meditation, yoga postures, *pranayama* breathing,

caloric restriction and such, are practices that involve the body as a whole. How could those be transduced into signals that activate regeneration at the tissue and cellular levels?

One proof of principle experiment showing that such signaling may have very precise local effects is referred to as "heterochronic parabiosis."[1,2] The design is straightforward: a young mouse and an old mouse are surgically linked to establish a single circulatory system. Wound healing is examined in each of these mice and compared with control mice of the same ages as those of the parabiotic pair. The results indicated quite clearly that sharing of a circulatory system rejuvenates the regenerative capacity of the older mouse in the pairing, while it simultaneously diminishes that capacity in the younger of the pair. Moreover, the effects at the single organs particularly examined (liver, skin) were cell and site specific, altering precise molecular signatures.

While nervous system control is unlikely to be a prime mediator of such effects—the speed of post-surgical cross-innervation being too slow for the findings—the other three mechanistic possibilities may well readily contribute to these effects. Humoral factors and trafficking cells readily disperse and mingle in the combined circulatory system as soon as the surgical shunts are complete. Also, the formation of a single somatic entity may result in a perhaps immediate mingling of electromagnetic fields or flux that might contribute to the observed effects.

The remainder of this essay will summarize other "proof of principle" examples of these mechanistic categories for global control and modulation of site-specific regeneration phenomena, and how they may link to specific C-Bp.

Humoral Effects on Regeneration

Melatonin is an example of humoral signaling which might function as a mediator between C-Bp and tissue regeneration and repair. Levels of this molecule are significantly elevated by meditation (reviewed in Ref. 3), and it has recently been found to possess not only powerful protective properties against oxidative and other forms of stress,[4] which may stabilize the intra-organ stem cell niche, but also play a direct role in stem cell and other regenerative processes.

For example, melatonin has been found to play an important role in regeneration of liver,[5] skin,[6,7] and hair[7,8] (and see literature review in Ref. 3), and recently melatonin receptors have been identified in neural progenitor and stem cells.[9] Quite intriguingly, recent studies have determined that both bone marrow[10,11] and hair follicles[7] are sites of significant numbers of melatonin receptors, as well as substantial synthesis of melatonin, and, in fact, concentrations are higher in the bone marrow than in the circulation or even the pineal gland.[10,11] In the liver, the highest melatonin concentrations in the body are in bile.[12] Since bile flows directly by the major intra-organ stem cell niche in the proximal branches of the bile ducts, which conduct the bile out of the liver, one must wonder about the possible actions of melatonin in the stem cell niche. We have recently identified expression of melatonin receptors in these structures (NDT, unpublished data). There is also some evidence that melatonin in the marrow specifically plays a role in regeneration of hematopoietic cells and bone[13] (reviewed in Ref. 14).

Even a non-exhaustive review reveals that melatonin promotes survival and/or regeneration not only in the tissues and organs already mentioned (liver, skin, hair, bone, and hematopoietic system), but also in brain,[15,16] eyes and ocular system,[17] heart,[18,19] gastrointestinal tract/endothelium,[20] neuroendocrine-reproductive axis,[21] and muscle.[22,23] Furthermore, while melatonin has been shown in quite a few studies to offer significant protection of healthy tissues from a range of offending agents (toxins, radiation, caloric and mechanical insult, etc.) through antioxidant, anti-apoptotic, and other mechanisms, and/or to stimulate regeneration in healthy tissues, it

has also been shown to selectively and differentially induce apoptosis in malignant cells (and tissues with other pathologies), including in the breast, lungs, stomach, endometrium, ovaries, cervix, prostate, GI tract, bone marrow, and others.[24–26]

That therapeutic effects can be derived from administration of melatonin (and thus may result from C-Bp derived up-regulation of endogenous melatonin production) comes from a series of not well-known studies from the Pierpaoli laboratory.[27–29] This group of investigators found that chronic melatonin administration, as well as cross-transplantation of pineal glands from young to old mice, led to a broad range of apparent aging delaying and/or reversing effects in behavior and physical appearance.[30] These effects probably can be seen in terms of tissue regeneration, but also in terms of aging.

Finally, although it is not well-known, melatonin also plays a role in regeneration in some of the "classic," *virtuoso* regenerators (although the literature is admittedly mixed), including in tail regeneration in the gekkonid lizard *Hemidactylus flavivindis*,[31] in limb regeneration in the fiddler crab *Uca pugilator*,[32] in regeneration generally in planaria,[33] and it has also recently been found to play a role in developmental cell proliferation in zebra fish.[34] Most recently, a study of tail regeneration in the lizard *Ophisops elegans macrodactylus* demonstrated that treatment with exogenous melatonin not only accelerated several—but not all—parameters of tail regeneration, but also enhanced the quality of the regenerated tail, by increasing the ratio of regenerated neurons to collagenous tissue.[35]

Several other relevant key molecules are also up-regulated by C-Bp (including caloric restriction, exercise, and/or specific forms of meditative practice), and should at least be mentioned in passing, although their significance is most likely substantive. Dehydroepiandrosterone (DHEA), increasingly known as a multiply cytoprotective, pleiotropic, "ubiquitous," antiaging steroid,[36–38] has also recently been found to stimulate stem/progenitor cell-based regenerative effects in the brain.[39] The salubrious effects of caloric restriction have been attributed to the maintenance of more youthful levels of DHEA and melatonin by conference participant George Roth,[40] while meditation has been found in some studies to increase circulating DHEA to levels more typical of individuals 5–10 years younger on average (reviewed in Ref. 41).

Some forms of meditation have also been found to enhance activity of the growth hormone/insulin-like growth factor-I axis, which is claimed to account for over 80% of postnatal growth,[42] and recently enhancement of activity in this axis has been found to promote stem and progenitor cell activation, proliferation, and mobilization[43–46] (although recent studies have also found potential aging accelerating effects of this axis[47]).

And, in addition, arginine vasopressin (AVP), circulating levels of which are increased during meditation by approximately 5–7 orders of magnitude, has been found to significantly increase myogenesis[48] and may also play a trophic role in both the peripheral nervous system[49,50] and the central nervous system (CNS),[50] where it is known to enhance learning and memory, including through up-regulation of other growth factors.[51] Constitutive nitric oxide may also crucially contribute to beneficial therapeutic, regenerative effects in a diverse range of pathologies and exert a "global healing effect"[52,53] and has been shown to be modulated through Zen meditation practices.[54]

Neural Mediation of Regeneration

Obviously, the cognitive practices under consideration at this meeting involve neurological functional changes (at least in part). Ways in which functional changes to the extraneural organs occur will be highlighted below, but there also may be direct neurogenic effects deriving from C-Bp.

One "arm" of traditional C-Bp regimens under consideration is the program of more or

less daily aerobic exercise principally in the form of repetitions of prostrations.[55,56] Daily yoga *asana* practice should function the same way. Recent research in exercise physiology has demonstrated that aerobic exercise stimulates stem and progenitor cell activation in several tissues, including brain.[57–59] Caloric restriction may also lead to increased neurogenesis, in addition to its effects on organism longevity.[59,60]

Another arm of the regimen consists of forms of meditation, which may vary in many ways, although most have in common the goal of significantly reducing the deleterious effects of stress (among other functions). As McEwen, Gould, and colleagues showed a number of years ago, stress can counteract the "normal" adult process of neurogenesis that typically occurs in brain areas such as the dentate gyrus,[61] while Elizabeth Blackburn and colleagues recently demonstrated that the deleterious effects of psychosocial stress on the organism actually appear to be mediated through depletion of telomerase and shortening of telomeres in a range of tissues![62,63]

Since corticosteroids are at least in large part responsible for the diminishment of brain progenitor cell proliferation,[61,64] the demonstrated corticosteroid-reducing effects of stress-reducing meditation[65,66] would therefore appear to be potentially capable of restoring precursor proliferation.[41] Similarly, the affect-enhancing meditation studied by Benson of Harvard[67,68] would also appear to lower corticosteroid levels,[69] may thereby be stimulatory for neurogenesis,[41] and may be related to the neurogenesis-stimulating effects of antidepressant medications studied by Duman at Yale and others,[70,71] especially since meditation has been shown to be as or more effective than antidepressant medication in the treatment of depression and related disorders.[72,73] Furthermore, cognitive activity—that is, enjoyable, but not stressful cognitive activity—has been associated with similar neurogenesis effects in the hippocampus,[59] and there are forms of meditation designed to promote cognitive activity (analysis, memorization, learning) during periods characterized as stress-free and associated with positive affective states.[41]

Importantly, a recent study on meditation conducted by a team of researchers from Harvard, MIT, and Yale found increased cortical thickness in meditation-related areas of the brains of meditators, in comparison to non-meditating controls,[74] a phenomenon which may also involve activation of brain stem/progenitor cells.[41] Furthermore, the possibility that CNS activity can influence stem cells outside the CNS has recently been highlighted by several studies, including a study by Bhatt et al.[75] demonstrating that epileptic activity, such as kindled seizure activity in the limbic system of lab animals, produced "hyperproliferation of bone marrow progenitor cells," while research by Steidl et al.[76] found that primary human CD34+ hematopoietic progenitor and stem cells express a previously unexpected range of active neuromediator receptors, including adenosine A2B, opioid kappa1 and mu1, CRH 1 and 2, 5HT 1F, and GABA-B.[77]

Thus, regeneration of CNS and tissues may be directly influenced by C-Bp and these effects in turn could possibly contribute to peripheral effects in other organs. Such peripheral effects are probably mediated by some of the humoral factors, as well as others, described above, but the CNS cells may exert direct control on regeneration through peripheral innervation. It has long been recognized that transplanted organs, with their severed connections to the peripheral nervous system have somewhat altered regenerative capacity, either by degree or by mechanism. For example, transplanted human livers have a diminished stem/progenitor cell response to injury compared to native livers in individuals with the same liver disease or injury.[78]

These clinical observations in human organ transplantation therefore suggest that innervation of solid organs is important for modulation of regeneration. Follow-up animal studies for the liver indeed confirm these observations, with up- or down-regulation of

sympathetic and parasympathetic nervous system input (by severing of nerves or pharmacologic manipulations) changing the ability to regenerate following liver injury.[78,79] Similar neural control of hematopoietic stem cells has more recently been definitively demonstrated.[80] In these experiments, pharmacologic or genetic alteration of norepinephrine leads to changes in G-CSF-induced osteoblast suppression, bone CXCL12 regulation, and hematopoietic stem and progenitor cell mobilization.

The precise mechanisms of the nerve control whereby these effects take place remain unclear, however. Three possible routes of nervous system control can be postulated: direct synaptic connections to the stem cells, direct innervation of an intermediate cell (e.g., the stromal cell component of the hematopoietic stem cell niche) which then modulates stem cell behavior, or releasing of neurotransmitters into the pericellular space or matrix. Evidence for all three of these has been found by our laboratory in examination of the normal liver stem cell niche.[81] Indeed, such direct contacts between peripheral nerves and the stem cells themselves form a concrete structure and image of the Mind-Body connection.

Bioelectric/Magnetic Influences on Regeneration

Of course, the CNS communicating with the rest of the body by nerve pathways is an electrochemical process, but bodies of all kinds (single or multicellular, plant or animal, etc.) are far more complexly electromagnetic entities on all levels of scale and many, if not all of these electromagnetic events may impact on aspects of regeneration. On the nanoscale, for example, it has recently been shown that electrons and electron holes migrate through the DNA helical structure, the former leading to repair of some mutagenic (e.g., UV) damage, the latter leading to displacement of oxidative injury from coding to non-coding regions.[82] All manner of ionic flow in and out of cells, including conduction of nerve pulses, is present on the cellular level. On the tissue level, ionic flux that can be modeled independent of the cellular substructure can also be demonstrated. An obvious example of this would be the heart, its global conduction from pacemaker cells serving to establish function and probably participating in repair. But less obvious examples exist as well, such as calcium waves that pass through the microscopic hepatic lobular subunits, perhaps with pacemaker hepatocytes responsive to different hormones, thereby integrating themselves on a community level for physiologic and regenerative tasks as well.[83]

As Paul Rosch, Marko Markov, and other pioneers have pointed out for a number of years, the importance of these and other forms of electrical and magnetic energy in fundamental life processes, including basic cell and tissue growth and regeneration, has not received the scientific recognition and attention deserved.[84,85] Although some recognition of "bioelectromagnetic medicine" as a valuable therapeutic modality has indeed occurred over the years, particularly regarding its empirically demonstrated efficacy in the treatment of bone fractures, soft tissue wounds, and more recently for a range of neurological disorders such as certain forms of pain and epilepsy, the full and appropriate integration of bioelectromagnetic energy data and theory into the predominant biochemical and molecular biology-based theoretical model has not been accomplished.[85]

Steps to correct this unfortunate situation have occurred in the form of several landmark publications. In particular, the quite recent publication in the leading journal *Nature* of a truly groundbreaking study by Colin McCaig and co-workers, which not only demonstrated again the critical role of electrical energy in tissue repair and regeneration, but even identified for the first time the (necessary) role of genes in these basic wound healing mechanisms.[86] These investigators showed, among other things, that increasing the strength of local electrical fields in the range of the endogenous wound electrical field, 42–100 $mVmm^{-1}$,

in a standard laboratory animal wound model, enhanced healing and that such enhancement was abolished by disruption of genetic pathways encoding for phosphatidlyinositol-3-OH kinase-gamma (PI3Kgamma). This work builds on a body of research pursued by these and other pioneering investigators that has been steadily growing, if without the recognition due it, for decades. And the other landmark publication to be noted here is the collection of state-of-the-art, authoritative essays brought together by Rosch and Markov in the recent volume, *Bioelectromagnetic Medicine*.[85]

How bioelectromagnetic processes may be influenced by C-Bp practices is difficult to identify with precision, in part because of a lack of careful definitions of terminology. A further tantalizing vein of research in this context relates to the use of C-Bp for manipulating putative forms of endogenous bioelectromagnetic (and possibly related forms of) energy, that have been claimed to exist in Asian and other systems in culturally endogenous or "emic" terms for many centuries.[87,88] For example, "external *qi* energy" produced by a "*qigong* master" and applied to the buffer used to culture cells was shown to have reproducible effects on monocyte phagocytic activity,[89] but the term "energy" in that context may or may not correlate with electromagnetic "energy" as Western scientists might use the term. So, in those experiments, application of *qi* was partially mimicked by microwave radiation and infrared laser pulse treatments, not explicitly electromagnetic of the sort briefly considered above for biological systems, though these may induce electron and/or ionic flux that are the same. On the other hand, effects of *qigong* or of acupuncture can sometimes be measured in terms of changes in conductivity, for example, which is clearly related to a conventional sense of bioelectromagnetic processes (though mechanisms remain quite uncertain).[90]

A number of contemporary studies in Asian countries have purported to determine that individuals may learn to stimulate, amplify, detect, and manipulate endogenous bioelectromagnetic, and/or other types of energy, through C-Bp for self-healing, healing, and other purposes.[87,88,91,92] A recent study conducted in the West, by leading bioengineering researchers who are colleagues of Dr. Rosch, has measured, in long-term experienced Chinese "*qigong*" practitioners, effects which are indexical of that portion of the electromagnetic spectrum belonging to applied magnetic fields.[93] This study, which measured levels of cell-free myosin phosphorylation *in vitro*, may one day be acknowledged as a breakthrough study in the West. Another study published by Korean researchers in a Western peer-reviewed journal, reported the results of a survey of Korean *qigong* practitioners which indicated that this practice accelerates wound healing, reduces inflammation, and, perhaps most notably, dramatically reduces or even eliminates the formation of scar tissue in wounds.[93] Such outcomes, if substantiated at the clinical experimental level, would clearly demonstrate the relevance of this energy and practice for regeneration.[94]

Cell Trafficking and Regeneration

The main traffickers in the body are the blood cells within the vascular spaces, including circulating cells of the immune system. While details of the roles played in regeneration by immune cells are only recently becoming clearer, several examples establish the principle. For example, an influx of natural killer T lymphocytes occurs in the liver following partial hepatectomy without which regeneration is significantly impaired.[95] The mechanisms whereby these lymphocytes encourage regeneration are unclear, though they may involve direct lymphocyte-hepatocyte contact with receptor-ligand mediated events. More interesting still is that in this same work, pharmacologic blockade or induction of sympathetic signaling modulates this process. Thus, we have one example of a network of effects that fall under the rubric of neuroimmunology.

Such neural-immune pathways have been described in greater detail by our colleague and fellow Conference participant Kevin Tracey[96,97] and incorporate afferent and efferent arms of an inflammatory/anti-inflammatory reflex mediated by fibers commencing peripherally with the vagus nerve, leading to a central "vaso-vagal control loop" in the nucleus of the tractus solitari (afferent) and then the dorsal motor nucleus (efferent), both within the brainstem. This readily presents possible links to C-Bp; for example, the anti-inflammatory arm of this pathway can be stimulated by activation of parasympathetic mechanisms, such as those mediating hypoarousal forms of meditation.[14,74] Thus, again, we have an example of global C-Bp practices with the potential for having signals transduced to a local level where regeneration will take place, if necessary.

These findings relate to other, recent key discoveries demonstrating that both immune/inflammatory augmentation and suppression can be classically conditioned in animals and humans in response to environmental stimuli, the CNS mediating the effects of cognitive states on inflammatory responses (recently reviewed in Ref. 98). One of us (NHS), at the time on leave from NIH (Neuroimmunomodulation Section), along with colleagues from the University of Alabama at Birmingham and the Gerontology Research Institute of Ancona, Italy, demonstrated augmentation of murine natural killer cell activity, leading to cancer regression, in a classical conditioning paradigm in which an immunologically neutral stimulus (CS), the odor of camphor, originally paired with an immune-stimulating drug, Poly I:C (US), then raises NK activity leading to tumor regression in the absence of the drug.[99–101] Conversely, several studies have demonstrated classical conditioning of immune suppression (CS-rose perfume smell, US-the documented immune-suppressing drug cyclophosphamide) leading to, for example, improvement in an inflammatory joint disease in rats,[102] and to improvement in autoimmune diseases in humans.[103–106] Although to our knowledge no study examining the relationship of conditioning to scar formation has been conducted, studies with a conditioning-like paradigm at Cornell Medical Center showed significant cognitively-mediated reductions in edema and infiltrate in response to experimental cutaneous wounding in humans.[107]

Other roles of trafficking cells, beyond those identified for immunocytes, are suggested by involvement of marrow cell involvement in repair of various tissues. Some of these migrate to sites of injury and, depending on the nature and severity of the injury, can differentiate into cells of the target organ, in what are referred to as "transdifferentation" or "plasticity through direct differentiation" events.[108,109] Work in our laboratory showed that such plasticity can occur with multiple tissues (blood and bone marrow, skin and adnexal structures, esophagus, stomach, small and large intestines, liver and bile ducts, lung and bronchi, i.e., mesodermal, ectoderm, and endodermal tissues), deriving clonally from a single cell.[110] Follow-up studies confirm robust and sometimes even therapeutic contributions to sites of injury through engraftment and direct differentiation in the liver,[111] gastrointestinal tract,[112] lung,[113,114] skin,[115] insulin-producing cells of the pancreas,[116] heart,[117] and kidney.[118] These findings, collectively, indicate that there is a degree of genomic plasticity in adult cells that had previously been undetected.[119–121] In such direct differentiation, the nuclear reprogramming is being conditioned by extracellular, micro environmental signaling.

Engrafting cells can also enter the target organs and participate in regeneration by fusing with preexisting cells.[108,109] This has been most dramatically demonstrated in the rescue from fulminant liver failure in a mouse model of hereditary tyrosinemia type I.[122] In this case, similar and dramatic re-programming of the adult nucleus is taking place, but the reconditioning is in response to cytoplasmic conditions (from the host cell cytoplasm and/or nucleus), in a physiologic correlate to the pioneering

heterokaryon experiments of Helen Blau and colleagues.[123]

That the engraftment of circulating, often marrow-derived cells contributes to restitution of the primary functional cell types of the organs is not the whole story however. The possible range of other functions is made clear by experiments with bone marrow transplantation in the setting of myocardial infarction. In addition to some degree of replacement of or fusion with cardiomyocytes, the engrafting cells also provide stromal support (fibroblasts, myofibroblasts) and endothelial components of the granulation tissue necessary for repair and some of these cells are further likely to produce cytokines and/or chemokines which also contribute.[124]

More surprising, and perhaps extraordinary, are the findings of conference participant Ellen Heber-Katz and colleagues who have shown that circulating cells elaborating tissue metalloproteinases (MMP-2 and -9) at the site of cardiac injury in the MLR mouse can prevent the formation of extensive scar.[125] The outcome is to promote regeneration without scar in a mammal of the kind that is seen in fish and amphibians with far greater regenerative potential.[125–127] That this is possible in humans, even without genetic mutation, is evidenced by rapid healing without scar demonstrated in medical anthropology studies of many communities around the world, usually associated with Samadhi-like states of consciousness.[128]

The C-Bp practices, we see, are generally systemic or global, but these may readily be transduced into local regenerative effects with quantifiable molecular, cellular, and tissue level effects. Possible mechanisms for such transduction from the global to the local include humoral and neurological signaling, trafficking of cells between tissue compartments, and bioelectromagnetic effects. While the first three have many possible mechanisms already being investigated, the last is only rudimentarily understood and it is in that area where not only has little investigative work been done, but the problem of terminology itself being so rudimentary inhibits the formation of adequate methodologies, within the Western and Asian traditions, let alone between them. (One of us [NHS] in collaboration with colleagues from the Jankovic Research Center in Belgrade, has been attempting to overcome some of these terminological as well as theoretical and methodological difficulties in investigations on the apparently reparative and regenerative effects of magnetic stimulation of the pineal gland.[129,130])

Nonetheless, while cultures and techniques may be varied, human bodies are more alike than dissimilar. This presentation should make it clear that great profit may be had for all participating cultures in establishing a common language, shared criteria for designing experiments and interpreting data, and cooperative goals for the promotion of tissue integrity and regeneration.

Summary

So we have shown that while skepticism regarding the possibilities for a productive meeting (metaphorically or actual) between Western medicine and biology and older healing and health practices of traditional cultures may be prevalent, there are many theoretical points of meeting and much experimental data to suggest that C-Bp of the latter may induce testable and reproducible phenomena for the former.

Conflicts of Interest

The authors declare no conflicts of interest.

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