

NEWS

Hippo-deficit adults regenerate cardiomyocytes after infarction

Ischemic heart disease is the leading cause of death worldwide.^[1] Recent advances in the conventional treatment regime, has reduced the mortality rates from myocardial infarction. However, these treatment regimens fail to address the primary problem of the cardiomyocyte's inability to respond to damage, by proliferation. Mammalian cardiomyocytes lose their ability to proliferate and exit the cell cycle during the first few weeks after birth.^[2] In contrast to humans, amphibians such as zebrafish and newts, are capable of regenerating up to 50% of the ventricle after mechanical excision by cardiomyocyte proliferation.^[3] Therefore, heart regeneration is possible only during embryonic development in humans, but this ability is lost during adulthood. Studies using animal models of myocardial infarction suggest that identifying and manipulating the endogenous mechanisms regulating mammalian cardiomyocyte regeneration, could result in complete functional heart recovery after infarction in adult mice. Hippo signaling, an ancient organ size control pathway, is a kinase cascade that inhibits developing cardiomyocyte

proliferation.^[4] Researchers from Baylor college of medicine and the Texas heart institute have found that Hippo-mutant hearts (blocking the Hippo pathway) were able to return to their full function after injury in adult mice.^[4] Thus, it is evident that the heart muscle can be coaxed for generating new muscle cells, which could be a breakthrough in cardiac regeneration research.

REFERENCES

1. Rosamond W, Flegal K, Friday G, Furie K, Go A, Greenlund K, *et al.* Heart disease and stroke statistics 2007 update: A report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2007; 115: e69–171.
2. Pasumarthi KB, Field LJ. Cardiomyocyte cell cycle regulation. *Circ Res*. 2002; 90:1044–54.
3. Laube F, Heister M, Scholz C, Borchardt T, Braun T. Re-programming of newt cardiomyocytes is induced by tissue regeneration. *J Cell Sci*. 2006; 119: 4719–29.
4. Heallen T, Morikawa Y, Leach J, Tao G, Willerson JT, Johnson RL, Martin JF. Hippo signaling impedes adult heart regeneration. *Development*. 2013 Dec;140(23):4683–90. doi: 10.1242/dev.102798.

Nanorobotics in brain drug delivery: A new hope

Blood brain barrier (BBB) is a highly selective permeability defense that shelters the brain from the changing metabolite concentrations in blood and provides an optimal chemical environment for cerebral function. There are several layers existing between blood and brain and each of these layers could potentially restrict the movement of solutes across them, which may be toxic to the brain.^[1] Researchers from the University of Montreal have found that the magnetic nanoparticles can open the BBB and deliver molecules directly to the brain.^[2] To date, about 98% of therapeutic molecules are unable to cross the blood-brain barrier.^[3] Presently, surgery is the only way to treat patients with brain disorders. However, some disorders are located in the brainstem, amongst nerves, making surgery impossible. Therefore, the major advantage of this technique is that

the barrier is temporarily opened at a desired location for approximately 2 hours, by a small elevation of the temperature generated by the nanoparticles when exposed to a radio-frequency field, without any inflammation of the brain.^[2] To open the BBB, the magnetic nanoparticles are sent to the surface of the BBB at a desired location in the brain, by using the MRI technology. The hyperthermia generated by the nanoparticles on reactance to a radio-frequency field creates a mechanical stress on the barrier, which can transiently increase the barrier permeability.^[2] It was demonstrated that the present technique did not disrupt the BBB integrity and was also not associated with inflammation.^[2] Thus, this technique allows a temporary and localized opening of the barrier for diffusion of therapeutics into the brain. Developing a local drug delivery

mechanism in human brains, could mean a breakthrough in the treatment and diagnosis of brain diseases using nanoparticles.

REFERENCES

1. Bauer HC, Krizbai IA, Bauer H, Traweger A. "You Shall Not Pass"-tight junctions of the blood brain barrier. *Front Neurosci.* 2014 Dec 3;8:392. doi: 10.3389/fnins.2014.00392. eCollection 2014.
2. Seyed Nasrollah Tabatabaei, Hélène Girouard, Anne-Sophie Carret, Sylvain Martel. Remote control of the permeability of the blood–brain barrier by magnetic heating of nanoparticles: A proof of concept for brain drug delivery. *Journal of Controlled Release*, 2015; 206: 49 DOI: 10.1016/j.jconrel.2015.02.027
3. Arijit Bhowmik, Rajni Khan, and Mrinal Kanti Ghosh, "Blood Brain Barrier: A Challenge for Effectual Therapy of Brain Tumors," *BioMed Research International*, vol. 2015, Article ID 320941, 20 pages, 2015. doi:10.1155/2015/320941

Vitamin D and cancer mortality

Vitamin D is classically known for its maintenance of bone mineral density. However, recently there is a growing body of evidence on the extra-skeletal roles of vitamin D.^[1] An adequate vitamin D status, as measured by serum 25-hydroxyvitamin D (25(OH)D) concentration, ranges between 95.4 to 235.32 nanomolar per liter (nmol/L). Several epidemiological studies have demonstrated an inverse relationship between lower serum 25 (OH) D concentration and mortality rates in cancer patients.^[2] Vitamin D levels are linked to better survival outcomes in several types of cancer. Especially, the link between serum 25 (OH) D levels and survival rate was found to be significant in patients with breast cancer, lymphoma and colorectal cancer.^[2] It has also been reported that women with lower baseline serum 25 (OH) D concentrations were at an increased risk of overall cancer mortality but not for the incidence of cancer.^[3] Although the exact biological rationale for the protective effects of vitamin D is unclear, findings from the animal studies suggest the stimulating role of vitamin D in the production of a known antagonist of c-myc, a protein critical in promoting cell proliferation and the transformation of pre-malignant to malignant cells.^[4] In addition, *in vitro* studies have also demonstrated the critical role of vitamin D in inhibition of tumor cell proliferation, angiogenesis and metastatic potential.^[5] Studies have reported that for every 30 nmol/L reduction in serum 25 (OH) D concentrations, there was an increased risk of cancer specific mortality by at least 30%, even after adjusting for age, gender,

seasonal changes, smoking status, cardiovascular and chronic kidney disease. Nevertheless, researchers have also found that, 10 nmol/L increase in serum 25 (OH) D levels is associated with 4 percent increase in survival rates in cancer patients.^[2,3] Thus, considering the widespread issue of vitamin D deficiency, physicians needs to closely monitor the vitamin D levels in patients diagnosed with cancer.

REFERENCES

1. Holick MF. High prevalence of vitamin D inadequacy and implications for health. *Mayo Clin Proc.* 2006 Mar;81(3):353-73.
2. Mian Li, Peizhan Chen, Jingquan Li, Rui'ai Chu, Dong Xie, Hui Wang. Review: The Impacts of Circulating 25-Hydroxyvitamin D Levels on Cancer Patient Outcomes: A Systematic Review and Meta-Analysis. *The Journal of Clinical Endocrinology & Metabolism*, 2014; jc.2013-4320 DOI: 10.1210/jc.2013-4320
3. Wong G, Lim WH, Lewis J, Craig JC, Turner R, Zhu K, Lim EM, Prince R. Vitamin D and cancer mortality in elderly women. *BMC Cancer.* 2015;15(1):1112. doi: 10.1186/s12885-015-1112-5. Epub 2015 Mar 8.
4. Salehi-Tabar R, Nguyen-Yamamoto L, Tavera-Mendoza LE, Quail T, Dimitrov V, An BS, et al. Vitamin D receptor as a master regulator of the c-MYC/MXD1 network. *Proc Natl Acad Sci U S A.* 2012;109(46):18827–32. doi: 10.1073/pnas.1210037109.
5. Zheng W, Wong KE, Zhang Z, Dougherty U, Mustafi R, Kong J, et al. Inactivation of the vitamin D receptor in APC (min/+) mice reveals a critical role for the vitamin D receptor in intestinal tumor growth. *Int J Cancer.* 2012;130(1):10–9. doi: 10.1002/ijc.25992.

VIEWS

Neuroprotective effects of caffeine against Parkinson's disease is gender specific

Parkinson's disease (PD) is the second most common neurodegenerative disorder with the progressive neuronal loss in the substantia nigra and associated decreased levels of dopamine in the striatum. PD afflicts 3% of the population older than 65 years. Caffeine's neuroprotective function in PD is attributed to its antagonistic action on adenosine 2A (A2A) receptors in the brain. Several studies have concluded that higher caffeine intake seems to be closely linked with reduced chance of developing PD. An prospective cohort study conducted in larger population of males (374,003 subjects) and females (345,184 subjects), demonstrates that increased consumption of coffee and other caffeinated beverages, progressively reduces

the risk of suffering PD. Especially, the markedly lower risk for developing PD was particularly strong in men, but was also present in females. In case of females, the protective effect of caffeine is observed only in menopausal women, those who have not received estrogen replacement therapy. Both estrogen and caffeine individually protect nigrostriatal dopaminergic neurons, but when combined, estrogen diminished the potency (rather than enhancing the efficacy) of the neuroprotective action of caffeine. Estrogen competes with caffeine for its activation of a protective pathway, effectively "occluding" the pathway of caffeine for neuroprotection. Thus, caffeine renders a gender specific neuroprotective effects against PD.

Facial misuse of topical steroids in India: Revisited

Topical corticosteroids (TC) are one of the most widely prescribed anti-inflammatory agents used for the treatment of steroid responsive skin disorders. Females aged 18-69 years accounts for about 75% of patients using TC and the sale of TC accounts for 82% sale of all topical drugs in India. Potent TC creams in combination with depigmenting agents, antifungals and antibacterials are being used irrationally by beauty clinics and self-medication by patients themselves. Most of the TC used by both women and men are listed under Schedule H drugs, which cannot be purchased without the prescription of a qualified doctor. But the reality is that, these TCs are being sold over-the-counter freely without any valid prescription by the dermatologist. Like fairness creams, TCs are freely available to the general population and in most instances, these are used as a depigmenting agent in combination with hydroquinone or mercury based bleaching creams. The abuse of TCs is mainly intertwined with fairness creams in our color

conscious society where people are obsessed with fair color due to various social and historical reasons. In a multicentric cross-sectional study, conducted at 12 centers in India, it was found that 59.3% of patients were using TC on the face without any doctor's prescription. Of the remainder, only 26.7% patients had used TC prescribed by a dermatologist. Thus, the combination of several factors like easy availability, lack of awareness regarding the side effects, obsession for fair skin, and poor access to dermatologists carves a favorable path for the misuse of TC in the community.

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