Real "Artificial" Gasoline

Do we currently have biologically-produced fuel? Of course we do! Gasoline in the US is currently supplemented with biologically-produced ethanol, which allows for the improvement of combustion and compliance with clean air standards (1). However, there are significant challenges to using ethanol as the principal fuel: it is expensive, results in significantly decreased mileage in cars, and requires the use of special engines (2). As of June 2010, using biologically-produced "artificial gasoline" is a new alternative. Commercial scientists identified the genes necessary to produce alkanes – the fat-like molecules that make up the majority of gasoline – in microorganisms that normally produce these macromolecules (3). These genes can be transferred to *E. coli*, resulting in a bacterium that eats simple sugars and produces gasoline. Most intriguingly, simple sugars can easily be obtained from crops such as corn, which the US grows abundantly due to government subsidies (4-5). Thus, a viable scheme for industrial production may be: grow corn, process it to obtain simple sugars, and convert these sugars into "artificial gasoline" via genetically modified bacteria. One thing is for sure: the age of oil will end without our consent, and we must be prepared to put something in its place. This may very well be that something. H

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▲ **Figure 1**: What does gasoline have to do with *E. coli*? Right now, not much. In the near future, the two may be closely linked.

credit: https://inglis.house.gov/issues.asp?content=sections/issues/current/high_gas_prices; http://www.niaid.nih.gov/SiteCollectionImages/topics/biodefenserelated/e_coli.jpg

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Haematopoietic Homeostasis: Regulation of Blood Stem Cell Metabolism

As multipotent blood progenitors, haematopoietic stem cells (HSCs) differentiate into adult blood cells and maintain homeostasis of the blood system by balancing stem cell self-renewal and differentiation, in addition to entering or exiting active cell cycling (1). While this capacity to respond to physiological changes possesses great clinical relevance—HSCs are used in bone marrow transplantation, as well as in the treatment of autoimmune diseases—the mechanisms that regulate HSC metabolism remain to be fully understood. Three recent findings together point toward the tumor suppressor, Lkb1, as a key player in regulating HSC energetics. Under normal conditions, Lkb1 is inactive and allows normal cellular proliferation; under stress, Lkb1 signals through the AMPK-mTORC pathway to suppress proliferation. To investigate the role of

news briefs

Lkb1 in blood formation, Nakada et al. removed Lkb1 function in mice and found that, after initial blood cell population expansion, all blood cell types died; furthermore bone marrow cells lacking Lkb1 function were incapable of repopulating the bone marrow of irradiated hosts. These findings indicate that Lkb1 plays critical roles in both cell cycling and in HSC survival (2). Contemporaneously-published findings by Gurumurthy et al. and Gan et al. provide further evidence that Lkb1 affects both HSC proliferation and programmed cell death (3, 4). To offer mechanistic insight into these findings, the three groups report on decreased mitochondrial function in mice lacking Lkb1 function as well as changes in mitochondrial morphology, which the authors suggest to be an attempt to compensate for decreased ATP production. Interestingly, despite Lkb1's previously-defined role in AMPK and mTORC signaling, its dramatic effect on HSC cycling and survival appears to be independent of this pathway, as deleting AMPK (3, 4) or blocking mTORC (2) produced no effect on HSCs. Collectively, these data provide novel insight into a sensitive and dynamic blood homeostatic regulatory mechanism and call upon future studies to answer questions regarding the described pathway and others that affect HSC metabolism. H

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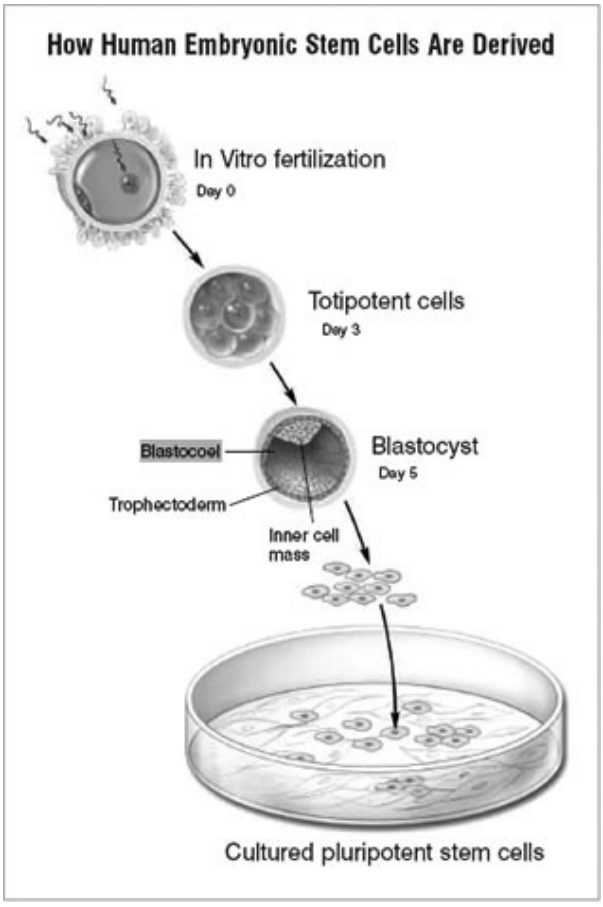
Generation of Induced Pluripotent Stem Cells Using RNA

Researchers at the Harvard Stem Cell Institute have recently reported a new method to create induced pluripotent stem (iPS) cells using RNAs (1). Induced pluripotent stem cells were first characterized by a group led by Shinya Yamanaka in 2007. The initial protocol for creating iPS cells involved using retroviruses to deliver four genetic factors (Klf4, c-Myc, Oct4, and Sox2) which would integrate into the genome. Expression of these genes can change mature, or fully differentiated, adult cell types into a pluripotent state. Pluripotent stem cells are capable of differentiating into any of the cell types in the body. The great potential of iPS cells lies in the fact that they are created from a patient's own cells, which means that iPS-derived cell types could be used to replace cells lost in patients with various diseases without issues of immune system rejection. One of the major problems has been to transform adult cells into the iPS cell state without causing potentially harmful genetic changes. Warren et al. developed an approach using synthetic messenger mRNA molecules containing specific modifications that allow them to evade natural cellular antiviral responses. Induced pluripotent stem cells derived using mRNAs, termed RiPSCs, were created with much greater efficiency than the older approach of iPS cell generation and demonstrated a closer resemblance to quintessential pluripotent cells, called Embryonic Stem (ES) cells, derived from blastocyst stage embryos. Scientists showed that RiPSCs have pluripotent potential by performing the differentiation of these cells into terminally differentiated muscle cells using another RNA molecule encoding the MyoD protein required for muscle cell development. RiPSCs represent a fundamental breakthrough in the field of regenerative medicine that brings stem cell technology closer to clinical use (1). H



▲ **Figure 1:** Human Embryonic Stem Cells

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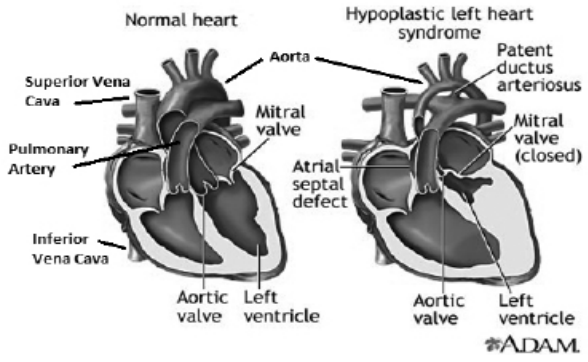
Debate over the Surgical Treatment of Hypoplastic Left Heart Syndrome



▲ **Figure 1:** Hypoplastic Left Heart Syndrome

Hypoplastic left heart syndrome is a heart defect that affects approximately three in ten thousand children and results in the malformation of chambers of the heart and vessels involved in establishing systemic circulation of oxygenated blood. Specifically, the left ventricle and aorta are significantly smaller than normal, an atrial septal defect allows mixing of blood from the left and right ventricles, and a defect links the pulmonary artery and aorta. Surgical intervention begins very early with the *Norwood procedure* to rebuild the aorta and to place a shunt between the pulmonary artery and the aorta to improve pulmonary blood flow. Three to six months later, the shunt is removed, but the superior vena cava and the pulmonary artery are left connected to maintain sufficient blood flow. Finally, between one to two years of age, the Fontan procedure is used to redirect blood from the inferior vena cava to the pulmonary artery (1). The first of these three surgeries is associated with the greatest mortality. A recent study published in the New England Journal of Medicine assessed the effects of using a right-ventricle pulmonary artery shunt (RVPA) as opposed to the traditional modified Blalock-Taussig (MBT) shunt during the Norwood procedure. The MBT shunt causes blood from systemic circulation to enter the pulmonary artery; this may result in reversed blood flow in the coronary arteries and aorta, leading to cardiac failure. The RVPA shunt has serious risks due to the trauma to the right ventricle; however, backward flow of blood from coronary arteries, called coronary steal, is reduced to ensure sufficient blood flow to the heart. The authors report that, although the RVPA shunt resulted in increased 12 month survival among infants would did not receive a heart transplant, there were higher numbers of serious cardiovascular complications during this one year period. In addition, there appears to be no improvement in survival after 12 months using the RVPA shunt compared to the MBT shunt (1). H

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1. Ohye, Richard G. Comparison of Shunt Types in the Norwood Procedure for Single-Ventricle Lesions. 2010. New England Journal of Medicine. 362:1980-1992.

credit: Adapted from http://www.nlm.nih.gov/medlineplus/ency/imagepages/19886.htm

The Yawning Hypothesis

Sitting in the dimly lit lecture hall of Science Center C, listening to the professor discussing, ad nauseum, about the difference between acetals and ketals, you inevitably succumb to the lure of sleep. But then realizing that the midterm is next week, you force open your eyes, stretch your arms above your head, and let out a big yawn in an effort to regain consciousness.

This common behavior, yawning, is observed in most vertebrate species and is a phenomenon that begins in early stages of development and persists until old age (1). However, the reasons for yawning have yet to be discovered. Although speculations have been rampant for centuries, with Hippocrates providing the first theory of yawning (to remove "bad air" from lungs) in the fourth century AD (1), lack of experimental data exist to explain the evolution and function of yawning.

One physiological hypothesis is that yawning allows for increased oxygen circulation in the brain and blood (1). Therefore, yawning should occur when there is an oxygen deficiency in the blood or brain; yet, behavioral observations have refuted this theory. Frequency of yawning was monitored in people who were exercising, and therefore in need of more oxygen, and people at rest (2). Frequency of yawning was also monitored in people exposed to gas mixtures with high levels of carbon dioxide and consequently low oxygen, compared to people exposed to the atmosphere (2). In both cases, the frequency of yawning was consistent between the two experimental groups (2). Thus, it seems unlikely that yawning plays a critical role in respiration and circulation (2).

There have also been other hypotheses for yawning – such as the brain arousal theory and ear pressure theory (3, 4). However, experimental results have failed to produce a persuasive physiological purpose for yawning in humans (1).

Interestingly, a social theory of yawns has also been proposed. Because yawning has been found to correlate with specific social circumstances, such as boredom, hunger, or stress, it has been suggested that yawning has a social mechanism (1, 5, 6). Further corroborations of this theory have been strengthened by the observation that the contagious effect of yawning in humans correlates to social skills transmitting emotions (7, 8). Humans with social interaction disorders such as autism or schizophrenia fail to show the same susceptibility to the contagious effect of yawning unlike healthy individuals (9).

To understand the physiological and even social purpose and effect of yawning, it might be necessary to first understand the molecular workings of the phenomenon. An investigation into the interactions between neurotransmitters, neuropeptides, hormones that have been identified to participate in the creation of yawns may elucidate a pathway that generates this trademark vertebrate behavior. H

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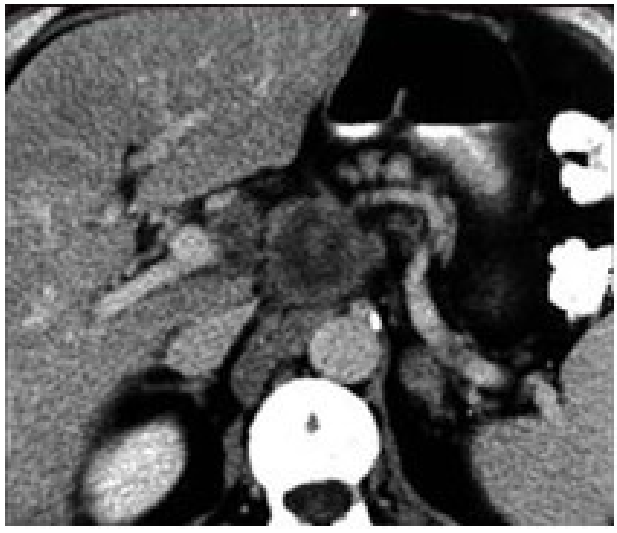
A New Intervention Window Appears in Battling Pancreatic Cancer at its Origins

With a cited five-year mortality rate of 97-98%, pancreatic cancer has so far presented formidable barriers to early disease identification and intervention (1). Two recent studies published in Nature offer insight into the long, genetic period of the developing disease state and project a new timeframe in which preventative treatment measures may be taken to halt cancer development. One study identified varied patterns of genomic instability among patients with metastatic pancreatic cancer and offered that such wide genetic variation resulted from evolutionary selection. However, pancreatic cancer is most commonly diagnosed at the metastatic state, a state in which the malignant tumor cells have divided and disseminated away from tissue of origin (2). A second study reported, at minimum, a decade-long period between the appearance of mutation and the origin of the non-metastatic cancer founder cell that subsequently gives rise to distant metastatic cells (2). The study concluded that the genetic diversity appearing in metastatic cells is present in the primary carcinoma cells. One identifiable genetic hallmark of pancreatic cancer that emerges well before tumor cell migration is fold-back inversion – a consequence of telomere loss (1). These findings offer a significantly prolonged time period for possible preventative therapeutic applications, well before the cancer progresses to the metastatic state (1, 2). While the science is not yet understood enough to dictate targeted interventional approaches, the studies show new approaches used by geneticists and medical scientists to address pancreatic cancer from a genetic angle. H



▲ **Figure 1:** CT Scan of a pancreatic tumor

credit: Adapted from http://www.nlm.nih.gov/medlineplus/ency/imagepages/1192.htm

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