Science Digest

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Links to malaria protection

Plasmodium falciparum (*P. falciparum*) is a leading cause of childhood malaria e.g. a child growing up in the Congo has a 22.5% cumulative risk of dying from malaria. Although sickle cell heterozygotes are the textbook example of protection against malaria there are obvious consequences with this untreated disorder. To complete their life cycle the parasites must bind to red cell receptors to enter the red cell and these are species dependent. *P vivax* binds to the Duffy receptor, which has been largely lost in African populations providing protection against *P vivax*. *P falciparum* targets glycophorins, which form the MNS blood group system. Recent research has identified that the glycophorin copy number variants were associated with resistance to *P falciparum,* which were higher in African populations (11%) compared to non-Africans (1.1%). One particular allele, the Dantu allele, is strongly associated with *P falciparum* resistance and is believed to represent human adaption to a *P falciparum* sub-species. The Dantu allele is restricted to East Africa suggesting it has only emerged recently.

The fetus has an active immune system

The fetal immune system has been regarded as passive but the quandary has been how does the fetus avoid maternal immune attack and how can it prepare for birth? Research from Singapore using fetal tissue has identified that the fetal immune system was active from as early as 13 weeks gestation producing a range of active immune cells as well as active dendritic cells. The research identified that the dendritic cells in culture produced more than the usual T-regulating cells and that different genes were switched on in the fetal dendritic cells than in adult dendritic cells. The fetal cells synthesized high levels of arginase-2, which breaks down argenine a key messenger for tumour necrosis factor alpha (TNF alpha), which triggers inflammation. The authors speculate that understanding the development of the fetal immune system could lead to a better understanding of adult immune system diseases as well as providing an explanation for some types of miscarriages.

New link between metabolism and immunology

Pre-beta-cell acute lymphoblastic leukemia (ALL) typically has mutations in transcription factor genes involved in beta-cell development. When leukaemia cells from 279 patients with pre-beta-cell ALL were analyzed, 209 had inactivating lesions in genes encoding beta-cell transcription factors) PAX-5; IK2F1; EBF1 and TCF3). Following chromatin-immunoprecipitation and sequencing all of the transcription factors bound to promoter regions of glucose uptake and influenced glucose metabolism as well as genes encoding negative regulators of . The changes resulted in associated reduction in glucose uptake and ATP depletion and it was subsequently identified that PAX-5 could act as a ‘gatekeeper’ to restrain glucose uptake and ATP supply in pre beta-cells. In addition the researchers found that PAX-5 and IK2F1 determined the responsiveness of beta-lymphoid ALL to determined the responsiveness of beta-lymphoid ALL to predispose treatment by inducing cell death by positively regulating NR3C1 levels. Overall, the research demonstrated beta-lymphoid transcription factors exert tumour suppression by limiting the supply of glucose and ATP to prevent malignant transformation of pre-leukaemic cells.

Does gut metabolism signal pathogenic bacteria protection?

It is well established that there is crosstalk between gut bacteria and the immune system. Part of the crosstalk involves bacterial derived metabolites. The short chain fatty acid, butyrate is a common metabolite that can bind to G-protein-coupled receptors on both colonocytes and immune cells leading to antimicrobial immune responses. Recent research from Belgium using an animal model has identified that butyrate directly influences colonocyte oxygen consumption through the beta-oxidation pathway leading to a symbiotic effect in normal gut by maintaining obligate anaerobes rather than facultative anaerobes such as pathogenic *Escherichia* and *Salmonella* by limiting the availability of oxygen in the gut, Additionally; gut nitrate is essential for facultative anaerobes, which is formed via nitric oxide synthase 2. The researchers identified that butyrate activates peroxisome proliferator-activated receptor-gamma (PPAR-gamma) in colonocytes which inactivated nitric oxide synthase 2 thereby reducing the nitrate production. In addition PPAR-gamma also activated beta-oxidation in macrophages. The researchers conclude that increased butyrate-producing bacteria in the gut, was associated with a lower risk of intestinal inflammation and gut-barrier dysfunction and that these interactions may have significance in obesity and diabetes mellitus.

A possible new bio-terrorism threat

Researchers in the USA have demonstrated that it is possible to use DNA sequences to hack in to analytical sequencing instruments. They developed a technique to encode malicious software in to strands of DNA. This then becomes a programme that corrupts gene-sequencing software. And takes control of the underlying computer. While this type of ‘attack’ is unlikely at present, computational biologists indicate that external sourced DNA could potentially be difficult to vet and that the hacking process has the potential to corrupt forensic and diagnostic DNA testing as well as gaining access to intellectual property resulting from DNA analysis. Although the design of the hacking sequence of the DNA was difficult the researchers indicate that the potential for such an attack is feasible. Currently the experimental hacking DNA hacks in to the memory of the computer running the compression software to run its own arbitrary commands.