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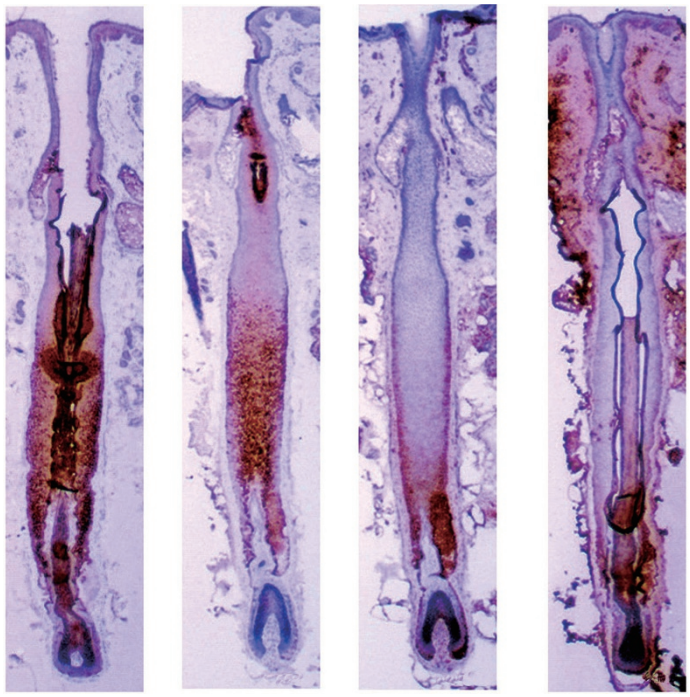

Mapping stem cells in the hair follicle

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There is growing interest in regenerative medicine, with many new studies focused on the identification of multipotential stem cells for regenerative cell therapies. The hair follicle is a complex structure that contains a reservoir rich in multipotent stem cells that can differentiate into all the component cells of the skin, including epidermal and follicular keratinocytes, sebocytes, and hair. These multipotent cells, which reside in a structure known as the "bulge," are known as hair follicle stem cells or follicular stem cells. While much elegant experimental work has been done in mice, only recently has attention been focused on the human hair follicle. To make a fine map of the hair follicle, Inoue and co-workers painstakingly dissected out individual hair follicles from human scalp skin and mapped the various cell populations using immunohistochemistry. They have identified nine subpopulations based on their expression profiles and performed a detailed analysis of the distribution of each cell type within the hair follicle. On the basis of their fine mapping, they have developed a simplified yet ingenious cell-sorting strategy that takes advantage of differences in cell size within different populations of bulge cells as well as differences in cell-surface antigens. Using this strategy, they isolated two populations of bulge cells that showed differences in clonogenic potential and proliferation. This excellent and thorough study has laid important groundwork for understanding the organization of the human hair follicle and the isolation of follicular stem cells for clinical applications.

Quantum leap in antigen detection?

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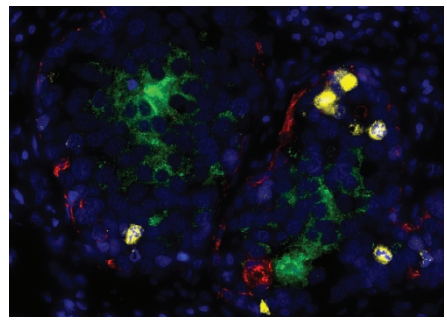
$CD44^{+}/CD24^{low}$ breast cancer cells have been reported to show "cancer stem cell" (CSC) characteristics. They are more tumorigenic in mice after primary inoculation and serial transplantation, and they have the capacity to recapitulate the morphologic and immunophenotypic diversity of the tumor from which they were isolated. $CD44^{+}/CD24^{low}$ CSCs have been reported to be enriched in breast cancer after chemotherapy, and it has been suggested that their survival is due to increased quiescence, providing a chemotherapy-resistant reservoir of tumor cells that can contribute to tumor recurrence. To further understand the role of $CD44^{+}/CD24^{low}$ CSCs in resistance to chemotherapy in breast cancer, Snyder and colleagues performed an analysis of CD44v6, an epithelium-specific CD44 antibody, and CD24 in formalin-fixed, paraffin-embedded sections of paired pre- and post-treatment breast cancer specimens. One of the most interesting aspects of this study is the use of quantum dot–labeled antibodies. With traditional immunohistochemical methods using light microscopy, no more than two antibodies can be viewed because of limitations in developing reagents. However, with antibodies linked to quantum dots, fluorescent semiconductor nanocrystals that have a constant excitation wavelength and a narrow emission spectrum proportional to their size, several different quantum dot–labeled antibodies can be visualized simultaneously by fluorescence-based imaging software, which enables the use of several antibodies. In the present study, three quantum dot–labeled antibodies were used on one section to simultaneously label cells with CD44v6, CD24, and Ki-67. This facilitated the labeling of subgroups of $CD44v6^{+/-}$ and $CD24^{+/-}$ breast cancer cells and investigation into whether different subgroups had different proliferative rates as measured by Ki-67 labeling. Although there are technical hurdles to be overcome, this technology appears to be very promising.



Fetal endothelial cells go for a swim in maternal blood pool

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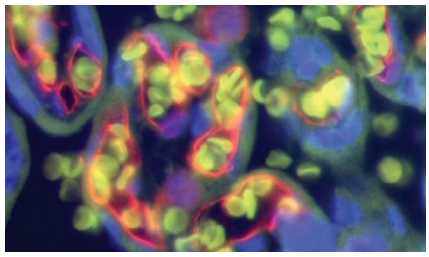

Many investigators have identified fetal cells in the maternal circulation, and there is mounting evidence that these cells can persist for decades. The fetal cells have features of progenitor cells in that they often home to injured tissues where they adopt differentiation appropriate to the various tissues. The intervillous space (IVS)—the maternal side of the placenta—contains maternal blood adjacent to fetal trophoplastic villi. To determine which fetal cells are transferred to the maternal circulation, Parant and colleagues hypothesized that the IVS would contain the largest proportion of fetal cells and thus be amenable to detailed characterization. They also took advantage of the presence of Y chromosomes from male fetuses to distinguish fetal from maternal cells. They discovered that 40% of the nucleated cells in the IVS were of fetal origin and most of the cells were CD34 positive. However, surprisingly, the CD34-positive cells were negative for CD117 and CD133 and positive for endothelial markers such as CD31 and von Willebrand factor. Hence, the major cell type that is transferred from the fetal to the maternal circulation is endothelial and not a hematopoietic stem cell as might have been expected. Future studies are required to define whether the fetal cells are endothelial progenitor cells or mature endothelial cells. Furthermore, additional characterization might reveal rare populations of other types of fetal cells. Nonetheless, it is clear that the IVS is a rich source of fetal cells that have made their way into the maternal circulation.

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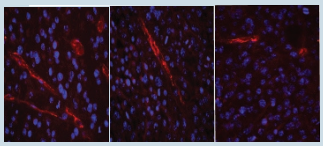
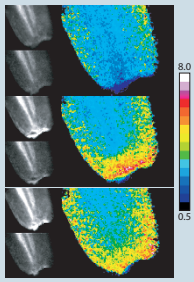
Learning new lessons from Down's syndrome



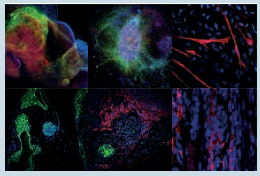
Epidemiological studies reveal that Down's syndrome individuals die from cancer at 10% of the expected rate. In a recent letter in *Nature*, Baek and colleagues report the discovery of a mechanism that explains this phenomenon. The Down's syndrome candidate region-1 (*DSCR1*) gene is one of 231 genes that is trisomic on chromosome 21. As a result of the extra copy of the *DSCR1* gene, DSCR1 is modestly overexpressed. Because DSCR1 is a negative regulator of vascular endothelial growth factor (EGFR)–calcineurin signaling in the endothelium, overexpression of DSCR1 results in decreased vascularization. In addition, they found that DYRK1A, encoded by *DYRK1A*, also located on the trisomic region of chromosome 21, collaborates with DSCR1 to suppress tumor vascularization. This exciting study not only serves to explain why Down's syndrome individuals have fewer solid tumors than expected but also highlights the EGFR–calcineurin signaling pathway as a potential target for therapeutic intervention for cancer prevention and therapy.

Nature 2009;459:1126–1130; doi:10.1038/nature08062

Dual functions for DUOX As described in a recent letter in *Nature*, Niethammer and colleagues devised an ingenious scheme involving fluorescent sensors in a zebrafish wound-healing model to show that hydrogen peroxide (H_2O_2) mediates the recruitment of leukocytes at the site of wounding. They showed that a gradient of H_2O_2 is created by dual oxidase (Duox), which recruits leukocytes to the wound. Given that DUOX has previously been implicated in protection from bacteria by reactive oxygen species–induced microbial killing at mucosal surfaces, this work suggests that DUOX has dual roles that also involve recruitment of leukocytes to wounded surfaces.



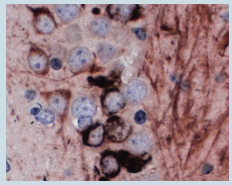
Nature 2009;459:996–999; doi:10.1038/nature08119



Patient, heal thyself Fanconi anemia (FA) is a rare, autosomal or X-linked, chromosomal instability disorder caused by mutations in any of 13 genes in the FA pathway. Patients with FA display chromosomal instability, develop bone marrow failure, and have an increased risk of developing cancer. Differentiated somatic cells can be reprogrammed genetically into induced pluripotent stem (iPS) cells, and therefore their potential in treating various diseases is almost limitless. The major advantage of treating patients with iPS cells is that rejection should not be an issue because they are essentially "self." Raya and co-workers asked whether they could correct the genetic defect in somatic FA cells prior to their being reprogrammed to generate iPS cells, and whether the latter could be used to generate disease-free hematopoietic progenitor cells. The answer was a resounding yes! While many details need to be worked out before this strategy can be used to treat FA patients, this excellent proof-of-principle study, recently reported in *Nature*, has shown the potential for iPS-based therapies, even in patients with genetic defects.

Nature 2009;459:53–59; doi:10.1038/nature08129

Novel experimental system for tauopathy Hyperphosphorylated tau comprises the filamentous intracellular inclusions of several neurodegenerative disorders and is therefore implicated as being central to their pathogenesis. Mice that express a mutant human tau isoform develop filamentous tau aggregates that are similar to those found in human tauopathies. In a recent letter in *Nature Cell Biology*, Clavaguera and colleagues describe their investigation into whether aggregation of tau could be transmitted. They injected brain extracts from mice that expressed mutant human tau that normally formed aggregates into the brains of mice that expressed a human tau isoform that did not normally form aggregates. They found that aggregates formed at the injection site and spread to other parts of the brain. This interesting new experimental system should facilitate the study of various aspects of the pathogenesis of tauopathy.



Nature Cell Biology 11;909–913; doi:10.1038/ncb1901