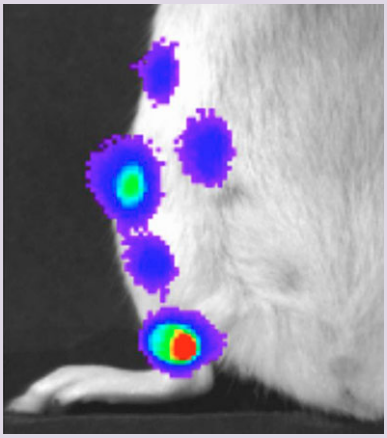

Shedding light on chronic Listeria infection

The pathogenic bacterium *Listeria monocytogenes* is the third most common cause of bacterial meningitis in neonates, and causes abortion and stillbirth. Additionally, sporadic outbreaks of listeriosis continue to claim lives, particularly in the very young and the elderly. Here, Jonathan Hardy and colleagues use in vivo bioluminescent imaging to visualize *L. monocytogenes* in mice. They found that live and attenuated forms of the bacterium reside in the bone marrow and persist for weeks following acute infection. The results draw attention to the bone marrow as a site of residual infection, both during and after treatment. Additionally, this study demonstrates that growth mechanisms still function in attenuated Listeria strains enabling the bacteria to colonize the bone marrow, which is important because these attenuated strains are being tested for their ability to induce anti-tumor immune responses in cancer patients.

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Costello syndrome modeled in zebrafish

Mutations in the Ras genes and signaling pathways are not only common in human cancers, but also cause several developmental disorders including Costello syndrome. Here, Cristina Santoriello and colleagues use zebrafish to study mutant oncogenic H-RAS during development and find that fish carrying the germline H-RAS mutation have several hallmarks of Costello syndrome. These include cranio-facial abnormalities and tumorigenesis, as is seen in the human disease. Furthermore, mutant fish exhibit cellular senescence in adult progenitor cells. Their work presents a new animal model for studying tumor development and Costello syndrome, and encourages further examination of cellular senescence underlying the age-related symptoms of Costello patients.

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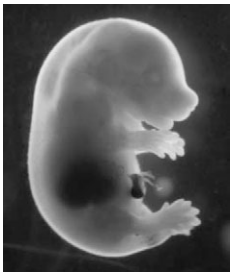
MDM2 variant found in tumors paradoxically promotes cell death



The tumor suppressor protein p53 is widely implicated in cancer. MDM2, a regulator of cell growth, can inhibit p53 and MDM2-A is one MDM2 splice isoform that is often detected in tumors. Here, Erin Volk, Katja Schuster and colleagues study the role of this truncated protein by creating transgenic mice that express MDM2-A in normal tissues. Although the mice were not prone to tumor development, heterozygote mice had a shorter life span than wild-type mice and homozygotes died shortly after birth. Studies using MDM2-A mice showed that, in contrast to the cancer-promoting activity of full-length MDM2 protein, MDM2-A activates p53, inhibits growth and enhances cell senescence. This work encourages further exploration of the unique roles of MDM2 variants in tumorigenesis and cell growth.

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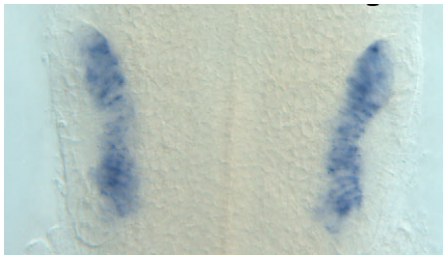
Basis of deafness in Waardenburg syndrome



The Waardenburg syndromes (WS) are rare genetic disorders described classically as neural crest syndromes and characterized by deafness and pigmentation abnormalities. WS type IV (WS4) is attributed to mutations in the *SOX10* gene, which regulates pigment cell development. Here, Kirsten Dutton and colleagues study otic vesicle development using a zebrafish model of WS4, the *colourless*/*sox10* mutant. WS4 patients and mutant fish display a similar spectrum of abnormalities in the ear, pigment cells and enteric neurons. Additionally, the researchers found that only a few neural crest cells contribute to the developing zebrafish ear, and therefore are unlikely to be wholly responsible for the resulting auditory deficits. Their work helps explain the origin of inner ear deficits that lead to hearing loss and vestibular problems in WS4 patients.

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Yeast model of lysosomal disorders

Juvenile neuronal ceroid lipofuscinosis (JNCL) is a lysosomal storage disorder in which neurodegeneration causes blindness, seizures, and mental and physical decline, eventually leading to death in early adulthood. *CLN3* mutations cause JNCL, but CLN3 function is not yet known. Here, Rebecca Haines and colleagues use the fission yeast *Schizosaccharomyces pombe* to model human JNCL, by expressing CLN3 mutations in the yeast orthologue Btn1p. The mutations caused vacuole deficits analogous to the lysosome deficits of lipofuscinoses and, for each *CLN3* mutation modeled, the severity of the yeast phenotype paralleled the severity of the human JNCL symptoms. The work presented here establishes a yeast model for mechanisms underlying JNCL and for screening novel therapeutic agents to treat this disease.

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