IFN-γ fights bacterial infection in zebrafish

Bacterial infection induces the innate immune response through cytokines such as interferon γ (IFN-γ). Zebrafish embryos lack adaptive immunity and may provide a simple model to study the innate immune system. However, it is not known whether zebrafish and mammalian cytokines are functionally conserved. Here, Dirk Sieger and colleagues show that two zebrafish isoforms of IFN-γ fight infection with *Escherichia coli* and the natural fish pathogen *Yersinia ruckeri*. Like mammals, IFN-γ in the zebrafish embryo regulates genes that are necessary to eliminate infection.

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This research article is freely accessible online.

Model for early stages of diabetes

The molecular events causing increased insulin resistance and secretion and early β-cell failure in diabetes are not well understood. Gema Medina-Gomez and colleagues define a mouse model, derived from insulin-resistant *ob/ob* mice, that lacks the nuclear receptor PPARγ2. Lipid profiles and other changes associated with early phase diabetes are evident in animals only 4 weeks old. β cells in the pancreas are initially protected from damage, showing increased insulin production and cell expansion. Thus, these mice demonstrate changes similar to humans in the early stage of diabetes.

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Endometriosis in MUC1Kras mice

Endometriosis can cause pain, infertility and ovarian epithelial tumors. Raluca Budiu and colleagues describe a double transgenic MUC1Kras mouse with inducible endometriosis. The expression of MUC1 increases in the ovaries as lesions appear. They suggest that the strong antibody response generated against MUC1 may promote tolerance to the antigen, leading to a reduction in immune competence that enables cancer progression. MUC1Kras mice could provide an in vivo platform for testing anti-MUC1 vaccines to treat endometriosis and prevent ovarian cancer.

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Myeloma RAG-2 knockout mice

In multiple myeloma, malignant plasma cells spread in the bone marrow, compromising hematopoiesis and creating soft lesions in the bone surface, which causes osteolytic bone disease. Jessica Fowler and colleagues made a mouse model lacking the immunoglobulin recombination enzyme, RAG-2. Inoculation of RAG-2 null mice with multiple myeloma cells causes tumor formation in the bone marrow and osteolytic bone disease, similar to human patients. This model is amenable to additional genetic modifications and deletion of another cancer-related gene, *Mmp9*, predictably alters the tumor microenvironment and facilitates cancer progression.

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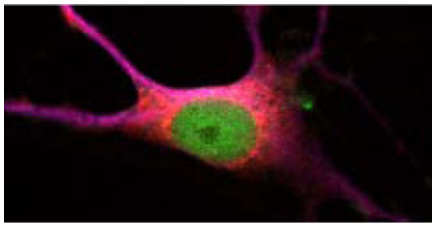
Ion channels in ataxia and epilepsy



Ion channels are gatekeepers, regulating neuronal excitability and neurotransmitter release. Genetic mutations to Kv1.1, a subunit of the potassium ion channel, are associated with episodic ataxia type 1 (EA1), with cerebellar dysfunction and uncontrolled motor activity that sometimes includes epileptic seizures. Joost Heeroma and colleagues show that Kv1.1 suppresses excitability in neurons and prevents neurotransmitter release. Mutations to Kv1.1 associated with episodic ataxia increase neurotransmitter release. Kv1.1 mutations variably affect neuronal excitability, providing some insight into the range of phenotypes associated with EA1 in patients.

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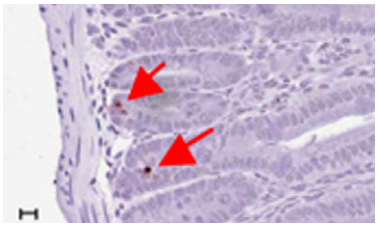
Restored telomeres in mice



Telomere changes are associated with disease, such as dyskeratosis congenita (DKC). Patients with DKC suffer from premature aging, bone marrow failure and a predisposition to cancer associated with impaired telomerase, disrupting normal telomere maintenance. Marie Meznikova and colleagues made a mouse with one functional allele of telomerase reverse transcriptase (Tert), a telomere-replenishing factor that maintains telomeres. Interbreeding of *mTert*-haploinsufficient mice for several generations restores telomerase function, suggesting corrective mechanisms for future telomere lengthening in mammals. Evoking these restorative pathways in human patients with DKC might limit some of the pathological effects of telomere shortening.

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