EDITED BY KRISTEN MUELLER AND MARIA CRUZ

DEVELOPMENT

Surprising Origins

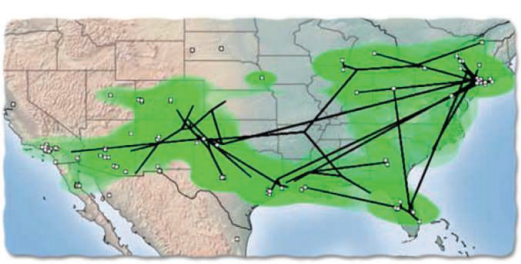
Similarities exist between the inner ear hair cells of humans and the lateral line hair cells of fish. Both respond to mechanical movements, from sound waves or water, respectively, and both arise from placodes of head ectoderm during early development. Humans, however, do not have a lateral line sensory organ. Many amniotes, including birds and some reptiles, have a paratympanic organ (PTO) near the middle ear that similarly contains hair cells and responds to mechanical distortion, suggestive of an evolutionary linkage between the lateral line and the PTO. O'Neill *et al.* now show that these ideas are close to the mark, but not right on. Studying the PTO in chickens, the authors show that the PTO derives from an ectodermal placode close by, but distinct from, the placodes that generate geniculate neurons and the lateral line. Although the PTO and geniculate placodes are so close as to almost blend together, they are nonetheless distinguished by their patterns of transcription factor expression and the developmental progressions that follow. The authors suggest that the PTO placode represents its own developmental module, subject to evolutionary trajectories independent of those of the lateral line. — PJH

Nat. Commun. **3**, 1041 (2012).

EPIDEMIOLOGY

The Right Time and Place

Spatial analysis, such as that used in epidemiology, is vulnerable to many errors, including that caused by spatial dependence or autocorrelation. For transmission of many infections, individuals need to be neighboring, and because the environment and behavior of nearby surroundings tend to be more similar than distant ones, neighbors will tend to be statistically dependent. This phenomenon causes complications for accurate epidemiological modelling. However,



pathogens can also be mapped in time, as well as place, and evolutionary biologists have developed phylogeographic methods to aid this sort of historical sleuthing. Given current concerns about the unexpected emergence of pathogens such as West Nile virus (WNV) in the United States, Pybus *et al.* have merged these concepts to develop an alternative, less error-prone approach. Taking data for WNV, they show how the diffusion coefficient and variation in the spatial spread of a pathogen can be estimated from genome data alone. This approach revealed that instead of a steady front of east-to-west dissemination of WNV, it progressed in fact by rare long-range movements, probably triggered by bird migration or anthropogenic transport of mosquitoes. These rare events leave a detectable phylogenetic footprint. Ignorance of this hitherto hidden heterogeneity has led in turn to considerable overestimation of the pathogen's basic reproductive number, R_0, a key parameter for estimating the epidemic potential of a pathogen. — CA

Proc. Natl. Acad. Sci. U.S.A. **109**, 15066 (2012).

BIOMEDICINE

The Good and the Bad in ALS

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease characterized by motor neuron death. Development of effective therapies will require an understanding of the molecular and cellular mechanisms that go awry in the disease—insights that often come from genetic approaches. Mutational analyses of rare hereditary forms of ALS have already implicated >12 culprit genes. Although several of these genes converge on common pathways, the overall view of pathogenesis remains incomplete.

Recent studies have uncovered two new genetic mutations that have an impact on ALS; interestingly, in one case the mutations appear to have a salutary effect on the course of the disease. Through exome sequencing of two large ALS families, Wu *et al*. discovered disease-associated mutations in the *PFN1* gene, which encodes the actin-binding protein profilin-1. In cultured cells, mutant profilin-1 formed insoluble aggregates and inhibited axonal outgrowth. Starting with a zebrafish model of ALS, Van Hoecke *et al*. discovered a disease-modifying gene called *EPHA4*, which encodes a receptor tyrosine kinase that interacts with ephrins, proteins involved in axonal repulsion. Inhibition of EphA4 signaling had beneficial effects in fish and rodent models of ALS. Importantly, two ALS patients who carried inactivating mutations in *EPHA4* showed uncharacteristically long survival. — PAK

Nature **488**, 499 (2012); *Nat. Med*. **18**, 1418 (2012).

CELL SIGNALING

Flip-Flop Messenger

CD38 is a transmembrane protein present on lymphocytes that appears to function in signal transduction. It has multiple enzymatic activities, two of which cause the generation of molecules that function to regulate the release of calcium from intracellular stores [cyclic ADP-ribose and nicotinic acid adenine dinucleotide

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