Prosser *et al*. propose that X-ROS signaling regulates Ca^{2+} signaling in the heart under normal conditions; in contrast, it may trigger abnormal rhythms in an injured or diseased heart. A future challenge will be to test whether the changes they observed in isolated heart cells also occur in the beating heart.

References and Notes

1. R. Knöll *et al*., *J. Mol. Med. (Berl.)* **81**, 750 (2003).
2. B. L. Prosser *et al*., *Science* **333**, 1440 (2011).
3. I. A. Williams, D. G. Allen, *Am. J. Physiol. Heart Circ. Physiol.* **293**, H1969 (2007).
4. M. G. Petroff *et al*., *Nat. Cell Biol.* **3**, 867 (2001).
5. G. Iribe, P. Kohl, *Prog. Biophys. Mol. Biol.* **97**, 298 (2008).
6. G. Iribe *et al*., *Circ. Res.* **104**, 787 (2009).
7. N. D. Ullrich, M. Fanchaouy, K. Gusev, N. Shirokova, E. Niggli, *Am. J. Physiol. Heart Circ. Physiol.* **297**, H1992 (2009).
8. D. M. Bers, *Nature* **415**, 198 (2002).
9. G. Meissner, *Curr. Top Membr* **66**, 91 (2010).
10. S. Györke, D. Terentyev, *Cardiovasc. Res.* **77**, 245 (2008).
11. B. L. Prosser *et al*. *J. Gen. Physiol.* **136**, 135 (2010).
12. J. J. Marengo, C. Hidalgo, R. Bull, *Biophys. J.* **74**, 1263 (1998).
13. G. Sánchez, Z. Pedrozo, R. J. Domenech, C. Hidalgo, P. Donoso, *J. Mol. Cell. Cardiol.* **39**, 982 (2005).
14. G. Sánchez *et al*., *Cardiovasc. Res.* **77**, 380 (2008).
15. C. I. Caldiz *et al*., *J. Physiol.* **584**, 895 (2007).
16. H. E. Cingolani, I. L. Ennis, E. A. Aiello, N. G. Pérez, *Pflugers Arch.* **462**, 29 (2011).

17. Research was supported by FONDECYT-FONDAP (grants 1501006 and BNI P-09-015F) and FONDECYT (grant 1110257).

10.1126/science.1212183

EVOLUTION

Mother Tongue and Y Chromosomes

A global picture is emerging of sex-specific transmission of language change in quite different regions and continents.

Peter Forster[1,2] and Colin Renfrew[3]

Some 6000 different languages are spoken in the world today, and tracing the prehistory of languages and of language change by means of genetic markers has long been a goal (*1*). However, this has proven to be a more challenging task than simply tracing colonizations. Nevertheless, a number of genetic studies over the past few years have started to address language and language change before recorded history. A correlation is emerging that suggests language change in an already-populated region may require a minimum proportion of immigrant males, as reflected in Y-chromosome DNA types. By contrast, the female lineages, as indicated by mitochondrial DNA (mtDNA) types, do not reflect the survivor language but represent more ancient settlement.

Chaubey *et al*. have found that in the Indian subcontinent, the Austroasiatic languages spoken by tribes such as the Munda show a high proportion (75%) of immigrant Y-chromosome DNA (a type called O2), which is generally found among peoples of East Asia, but predominantly (75 to 100%) local Indian mtDNA types (*2*) (in humans, mtDNA is inherited from the mother) (see the figure). Similarly, the study found that another major language family, Tibeto-Burman in northeastern India, coincides with a high proportion of immigrant East Asian Y-chromosome O3 types, which are generally found in populations of southeastern Asia. The East Asian mtDNA is rarer in Tibeto-Burman speakers residing in India.

A compatible observation has recently been made by Stoneking and Delfin (*3*), who noted that in East Asia, a patrilocal residence pattern (where women rather than men change residence upon marriage) favors geographic stability of the male lineage. This may reflect the migration of men and women (and their language) to an already populated area, but once settled, the women intermarry with men from neighboring populations and move to their villages. In this scenario, the immigrant men remain, and the language therefore stays in the same place as the immigrant Y chromosomes. And in Africa, Wood *et al*. (*4*) and de Filippo *et al*. (*5*) found that Bantu and other Niger-Congo languages correlate well with Y-chromosome types (indicating male lineages), whereas mtDNA types (associated with maternal descent) correlate not with language but with geography in Bantu-speaking areas.

Sex-specific transmission of language change may be a feature when the mechanism of change is by farming/language dispersal (*6*). This dispersal hypothesis describes how language change can be linked to the early spread of food—domesticated animals and plants—by farmers speaking a protolanguage. In the Americas, language replacement in the course of postulated farming dispersal has been found to correlate in the Uto-Aztecan language family with Y-chromosomal DNA variation but not with mtDNA variation (*7*).

As for the immigrant Indo-European and the presumably indigenous Dravidian languages in India, there is one major candidate genetic marker for immigration from the northwest. It is a Y-chromosome DNA

Language transmission. Glossogenetic studies relate Y-chromosome DNA types with language in the indicated regions. Such correlation is not observed for mtDNA, which is inherited from the mother. "Melanesian" designates non–Malayo-Polynesian languages in New Guinea, where Malayo-Polynesian is spoken in coastal pockets. The hatched region shows Bantu as a branch within the Niger-Congo language family.

CREDIT: B. STRAUCH/SCIENCE

[1]Murray Edwards College, University of Cambridge, Cambridge CB3 0DF, UK. [2]Institute of Forensic Genetics, 48161 Münster, Germany. [3]McDonald Institute for Archaeological Research, University of Cambridge, Cambridge CB2 3ER, UK. E-mail: pf223@cam.ac.uk

Published by AAAS

type (J2a) rather than an mtDNA type, and its immigrant status is suggested by its presence at 10 to 20% frequency in high castes, both in Indo-European speakers and farther south among Dravidian speakers, and its near-absence in lower castes or "tribals" (*8*).

Perhaps the most striking example of sex-biased language change comes from a genetic study on the prehistoric encounter of expanding Malayo-Polynesians with resident Melanesians in New Guinea and the neighboring Admiralty Islands (*9*). The New Guinean coast contains pockets of Malayo-Polynesian–speaking areas separated by Melanesian areas. The presence of Malayo-Polynesian mtDNA (at local frequencies of 40 to 50%) is similar in these areas regardless of language, whereas the Malayo-Polynesian Y chromosome correlates strongly with the presence of Malayo-Polynesian languages. Mirroring the situation in the Indian upper castes, the presence of immigrant Malayo-Polynesian Y-chromosome DNA is modest, at frequencies of 10 to 20%, in the Malayo-Polynesian pockets, but this figure is still an order of magnitude higher than in the non–Malayo-Polynesian areas.

In Europe, a genetically researched protohistoric case of language dominance is the colonization of Iceland from 874 C.E. by Scandinavian Vikings and abducted women from the British Isles (*10*, *11*). Icelandic mtDNA today is mainly British, while the Y chromosome is predominantly Scandinavian, as indeed is the Icelandic language. A contrasting case is found in Greenland, where both the mtDNA (*12*) and the language today are nearly pure Eskimo, while half the Y chromosomes are European (*13*), evidently from contact with male European whalers over the centuries. The Greenlandic and Dravidian cases suggest that a Y-chromosomal signal may be a necessary factor, but not a sufficient one, as a predictor of language.

If the emerging correlation is confirmed, there should be underlying causal factors of a social nature. It may be that during colonization episodes by emigrating agriculturalists, men generally outnumbered women in the pioneer colonizing groups and took wives from the local community. When the parents have different linguistic backgrounds, it may often be the language of the father that is dominant within the family group. It is also relevant that men have a substantially more variable number of offspring than do women, as has been recorded both in prehistoric tribes such as the 19th- and 20th-century Polar Eskimo from Greenland (*14*) and in historic figures such as Genghis Khan (1162 to 1227 C.E.), whose Y chromosome is presumed to be widespread across his former Mongol empire and is carried by 0.5% of the world's male population today (*15*). Prehistoric women may more readily have adopted the language of immigrant males, particularly if these newcomers brought with them military prowess or a perceived higher status associated with farming or metalworking.

References

1. L. L. Cavalli-Sforza *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **85**, 6002 (1988).
2. G. Chaubey *et al.*, *Mol. Biol. Evol.* **28**, 1013 (2011).
3. M. Stoneking, F. Delfin, *Curr. Biol.* **20**, R188 (2010).
4. E. T. Wood *et al.*, *Eur. J. Hum. Genet.* **13**, 867 (2005).
5. C. de Filippo *et al.*, *Mol. Biol. Evol.* **28**, 1255 (2011).
6. P. Bellwood, C. Renfrew, *Examining the Farming/Language Dispersal Hypothesis* (McDonald Institute, Cambridge, 2002).
7. B. M. Kemp *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **107**, 6759 (2010).
8. S. Sengupta *et al.*, *Am. J. Hum. Genet.* **78**, 202 (2006).
9. M. Kayser *et al.*, *Mol. Biol. Evol.* **25**, 1362 (2008).
10. A. Helgason *et al.*, *Am. J. Hum. Genet.* **68**, 723 (2001).
11. P. Forster *et al.*, in *Traces of Ancestry*, M. Jones, Ed. (McDonald Institute, Cambridge, 2004), pp. 99–111.
12. J. Saillard *et al.*, *Am. J. Hum. Genet.* **67**, 718 (2000).
13. E. Bosch *et al.*, *Hum. Genet.* **112**, 353 (2003).
14. S. Matsumura, P. Forster, *Proc. Biol. Sci.* **275**, 1501 (2008).
15. T. Zerjal *et al.*, *Am. J. Hum. Genet.* **72**, 717 (2003).

10.1126/science.1205331

NEUROSCIENCE

How Many Cell Types Does It Take to Wire a Brain?

Microglia play an important role in the maturation of synaptic circuits in newborn mice.

Richard M. Ransohoff[1] and Beth Stevens[2]

Microglia, highly mobile immune cells that reside in the central nervous system, are traditionally viewed as "barometers" of the brain because they rapidly respond to cellular damage caused by injury and disease by engulfing and cleaning up debris (*1*). Imaging studies, however, have revealed that microglia are also ceaselessly active in healthy brains, and other studies have shown that this activity is often associated with synapses, which move signals between neurons (*2*–*4*). Despite these intriguing observations, the function of microglia at healthy synapses has been elusive. On page 1456 of this issue, Paolicelli *et al*. (*5*) help pin it down. They demonstrate that microglia are involved in the development of brain wiring in newborn mice and that disrupting microglia-synapse interactions delays the maturation of synaptic circuits. The finding offers insight into the mechanisms underlying synapse maturation and into brain diseases in which synaptic connectivity is altered.

In the brain, microglia are the only cells that express the fractalkine receptor CX3CR1; it specifically binds the chemokine fractalkine CX3CL1, which is expressed by neurons (*6*). Fractalkine signaling often modulates the activation of microglia response to injury or disease (*7*, *8*). In genetically modified knockout (KO) mice unable to produce the fractalkine receptor ($Cx3cr1^{KO}$), there is a transient decrease in microglial density in several developing brain regions, including the hippocampus, a region critical for learning and memory. To determine whether this decrease affects the development of hippocampal synapses, the researchers compared $Cx3cr1^{KO}$ mice with age-matched controls, looking for anatomical, electrophysiological, and behavioral abnormalities associated with disrupted synaptic maturation.

They observed that newborn $Cx3cr1^{KO}$ mice had an increased density of hippocampal spines, small protrusions from a neuron's dendrite that receives synaptic input from presynaptic axons. This observation is consistent with a role for microglia in "pruning" of unneeded spines in normal mice during brain development. Indeed, the researchers observed postsynaptic-density (PSD) immunoreactivity within microglia cytoplasm, suggesting that microglia engulf and remove spines during this period of synaptic remodeling. In addition, electrophysiological and behavioral experiments demonstrated a delay in the maturation of hippocampal synapses in the KO mice. For example, elec-

[1]Neuroinflammation Research Center, Lerner Research Institute, Cleveland Clinic, Cleveland, OH 44195, USA. [2]Department of Neurology, Children's Hospital, Harvard Medical School, Boston, MA 02115, USA. E-mail: ransohr@ccf.org; beth.stevens@childrens.harvard.edu