organize the empirical-theoretical work. Doing all three, which often involves learning just enough math to collaborate effectively with theoreticians, is career enhancing and fun. In particular, as noted above, exciting new fields often blaze forward empirically, driven by applied needs or new technologies, and accumulate case studies that reveal variation — unexplained patterns — but without the concomitant development of a cohesive conceptual framework. When you spot one of these opportunities, identify good collaborators and jump in. Look for ways to develop hot topics in novel directions. Again, be integrative. Many advise integrating across levels of study: for instance, integrating (epi) genetics/genomics, neuroendocrine/physiological mechanisms, behavior, and ecology. This is clearly worth doing, though in many cases logistically challenging. I add my encouragement to be integrative in the sense of bridging conceptual fields — as we enjoyed doing in the early days of studying animal personalities. To spot opportunities and build new bridges, I encourage what might be obvious: read widely; go to lots of seminars, including ones somewhat outside your core interests; take notes at seminars, actively highlighting new ideas and conceptual bridges; talk to people; trade ideas; and build your intellectual network. Of course, you cannot do it all, but do your best to hone in on a topic and system that make both you and others visibly super excited.

For a somewhat odd final question, what is the most interesting factoid about your long career? A recent UC Davis merit review required me to summarize my research program(s), including my mentoring over the years, and I discovered that, after 39 years as a university faculty member, my lab has had 39 postdocs and completed 39 PhDs. Perhaps obviously I am delighted and proud to have such a large and accomplished academic family.

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Quick guide

Teneurins

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What are they? Teneurins are evolutionarily conserved type II transmembrane proteins. They comprise a small intracellular amino terminus, a single transmembrane domain, and a large extracellular carboxyl terminus containing multiple conserved domains that mediate their interaction with other proteins (Figure 1). They are enriched in the nervous system where their functions have been best characterized.

How were they discovered? Attempts to find *Drosophila* homologs of the extracellular matrix protein tenascin in the early 1990s led to the discovery of two proteins, Ten-a and Ten-m. When vertebrate homologs of Ten-a and Ten-m were identified in the late 1990s, these proteins were given the name ‘Teneurins’ to combine their two features: tenascin-like and enriched expression in neural tissues.

Which animal species are Teneurins found in? Teneurins are present in single cell choanoflagellates and bilaterians, but absent in sponges and cnidarians, likely due to gene loss. Worms have one Teneurin (Ten-1), flies have two (Ten-a and Ten-m), and chickens, rodents, and humans all have four (Ten1–4).

What kinds of domains do they have? All Teneurins share multiple extracellular domains: EGF-like repeats that mediate Teneurin dimerization in *cis*; a beta propeller region that occurs in multiple forms due to alternative RNA splicing and affects Teneurin homophilic binding strength; a YD repeat region (enriched for tyrosine and aspartate) containing a binding site required for heterophilic protein interaction; and a Tox domain resembling a prokaryotic nuclease that encapsulates the YD repeat region. The intracellular domain of Teneurins is less conserved between species and isoforms. It remains unclear how these differences in the intracellular domain is related to protein function.

Where are they found? Teneurins are enriched in developing and adult nervous systems. Different Teneurins can often be found in complementary patterns. The same Teneurins are sometimes expressed in interconnected neurons. Teneurin proteins tend to be concentrated in axons, dendrites, and synaptic regions. Teneurins are also expressed in non-neural tissues.

What do they do? Teneurins are best studied in the context of neural circuit wiring. In *Drosophila*, matching expression patterns of Teneurins instruct synaptic partner matching in the olfactory and neuromuscular systems. In both mouse and zebrafish, Ten3 is involved in wiring of the visual system. Mouse Ten3 also regulates target selection of hippocampal axons. Other reported functions of Teneurins include regulation of synaptic organization, neuron–glia interaction, and neuronal migration. In non-neural tissues, *Drosophila* Ten-m regulates planar cell polarity at epithelial compartment boundaries during convergent extension.

Who do they interact with? Studies in cell culture provided evidence that vertebrate Teneurins can mediate homophilic interactions. In the fly olfactory system, the matching expression of Ten-a and Ten-m in synaptic partners and genetic loss- and gain-of-function studies support a homophilic attraction mechanism for instructing synaptic partner matching.

Heterophilic interactions between vertebrate Teneurins and Latrophilins, members of the family of adhesion G-protein-coupled receptors, have been reported by multiple groups in the early 2010s. Since then, Teneurin–Latrophilin interactions have been implicated in synapse formation, axon guidance, synapse specificity and neuronal migration. Structural studies of the Teneurin–Latrophilin complex revealed the exact regions of each protein critical for their interaction: the lectin domain for Latrophilins and YD repeat region for Teneurins.

Both homophilic and heterophilic interactions are required in target

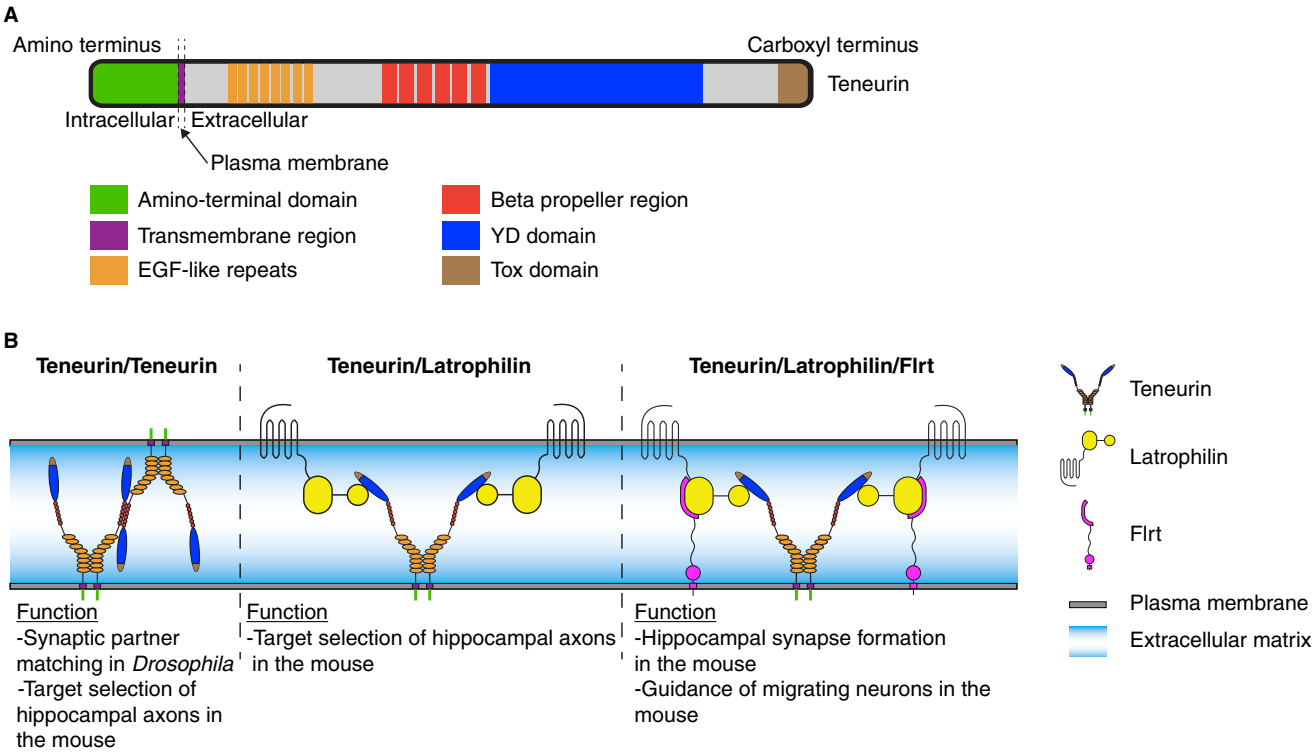

Figure 1. Teneurin domains and interacting partners.
(A) Teneurins contain a small intracellular amino-terminal region and a large extracellular carboxy-terminal region containing multiple conserved domains across all species. (B) Cartoon depiction of Teneurin interactions. Teneurins mediate homophilic interactions (left) and heterophilic interactions (middle and right) to regulate neural development and function.

selection of hippocampal axons: Ten3/Ten3–mediated homophilic attraction and Ten3/Latrophilin-2–mediated heterophilic repulsion cooperate to ensure precise target selections of CA1 axons in the subiculum. Ten3 and Latrophilin-2 are expressed in complementary subregions across multiple synaptically connected regions.

A separate extracellular domain of Latrophilins binds Flrts, a transmembrane protein family with extracellular leucine-rich repeats. The tripartite complex of Teneurins, Latrophilins, and Flrts is implicated in regulating hippocampus synapse formation and repulsion during neuronal migration.

Does mutation of Teneurin genes cause human disease? In humans, mutations of Teneurin genes have been associated with multiple nervous system disorders: Ten4 is associated with bipolar disorder, Ten3 with eye malformation, and Ten1 with a complete loss of smell. In addition, mutation, chromosomal alteration and deregulation of Teneurin expression have been associated with multiple tumor types; these changes have been proposed as new diagnostic and prognostic biomarkers.

Where can I find out more?

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