# A sibling conflict that gets on your nerve

Sisters or brothers are often your keenest competitors before they become your closest friends later in life. This sibling conflict, so fundamental and pervasive in human nature, is a popular theme from ancient mythology to popular culture. Until mutual understanding and reconciliation are achieved, conflict is best minimized by avoiding contact, which is learned after unhappy encounters in sibling rivalry. Intriguingly, branches called dendrites from the same nerve cell (neuron) also largely avoid one another when they grow in the same surroundings. This “self-avoidance” enables neuronal branches to maximize coverage of the sensory territory while minimizing crossover between sibling dendrites.

“If you take a movie of growing dendrites in live animals, dendrites kiss and then back off after the brief encounter,” said Chien-Po Liao, a Ph.D. candidate in the laboratory of Chun-Liang Pan, M.D., Ph.D., at the Institute of Molecular Medicine, National Taiwan University. Dendrites from different types of neurons cross and do not avoid each other, suggesting that dendrites can somehow distinguish self (same) from nonself branches. A handful of proteins that exist on the surface of dendrites are important for self-avoidance, but how these molecules enable dendrite repulsion remains a mystery.

The model organism used for research in the Pan laboratory is a tiny soil-living roundworm called *Caenorhabditis elegans* (*C. elegans*), and its body transparency facilitates the observation of neuronal structures in vivo. Chien-Po studied a membrane protein called MIG-14/Wntless, whose only known function is to control the secretion of Wnt signaling molecules. Sibling dendrites in worms that lack MIG-14/Wntless show more frequent contact, implying that MIG-14/Wntless is important for dendrite self-avoidance. “I then assumed that Wnt signaling molecules are also important,” Chien-Po recalled, “but to my surprise,

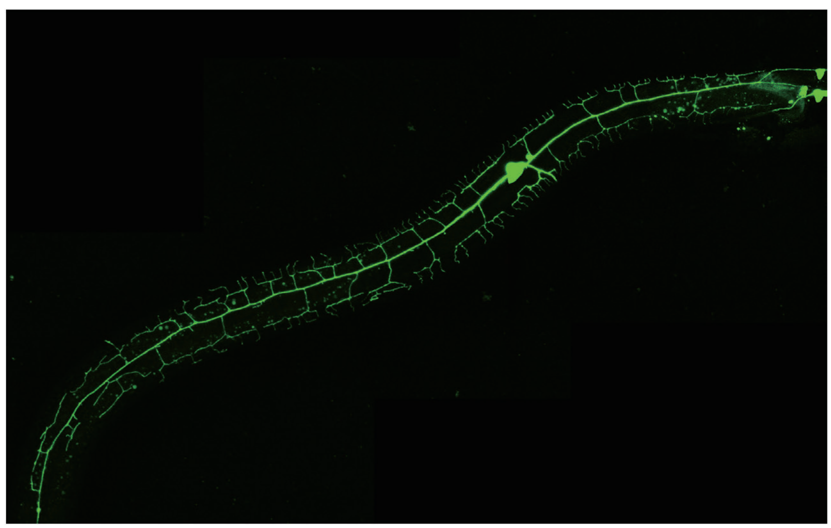

**Figure 1.** ***Caenorhabditis elegans*** **(*C. elegans*)**

worms that lack Wnts show normal dendrite self-avoidance." Dr. Chun-Liang Pan studied MIG-14 when he was a graduate student at the University of California, Berkeley, some ten years ago. "This is the first time people have learned that MIG-14 does something unrelated to Wnt signaling, which is important news in the field," said Chun-Liang.

At approximately the same time, Lakshmi Sundararajan and David Miller at Vanderbilt University, USA, were studying how proteins that support neuronal structures can also retract sibling dendrites after contact. This paradoxical idea arose in part from their observation that F-actin, a filamentous protein that allows the cell membrane to stretch into diverse shapes, shows a local burst in intensity at the dendrite tips, and this F-actin burst is important for dendrite self-avoidance. The Pan laboratory discussed the subject with the Miller laboratory at the International *C. elegans* Meeting, and Chien-Po decided to explore whether MIG-14/Wntless controls dendrite self-avoidance by signaling the F-actin cytoskeleton. Indeed, in worms that lack MIG-14/Wntless, the F-actin burst at the dendrite tips was diminished, providing a molecular basis by which MIG-14/Wntless ensures dendrite self-avoidance. The Pan laboratory reported their findings in the journal *Neuron*.

Some may dismiss the worm research, but in a collaboration with Hsun Li and Dr. Cheng-Ting Chien at the Institute of Molecular Biology, Academia Sinica, the Pan laboratory demonstrated a similar function of Wntless in the dendrites of *Drosophila* (fruit fly). It is therefore unsurprising if Wntless also controls dendrite self-avoidance in mammals, but genetics and live imaging in such animals are much more challenging. "We are blessed by the Imaging Unit of the First Core Facility at the College of Medicine," said Chun-Liang, citing the expertise of the microscopic specialist, Hwa-Man Hsu, as instrumental in the success of the project. "Nature unveils its elegant choreography of dendrite development before your eyes. Every time I watch the video, I am filled with nothing but awe."

**References**

Liao, C., Li, H., Lee, H., Chien, C., & Pan, C. (2018). Cell-autonomous regulation of dendrite self-avoidance by the Wnt secretory factor MIG-14/Wntless. *Neuron*, *98*(2), 320-334. doi:10.1016/j.neuron.2018.03.031

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