Researchers report mechanism for cellular signal amplification by scaffold proteins

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Cellular signaling pathways involved in everything from the proliferation of fatty tissue to the death of neurons in the brain are tightly regulated by "cascades" of sequentially activated enzymes, MAP kinases. These enzymes are held in the proper position for activation by "scaffold" proteins.

This model does not explain, however, how the cellular signal is

amplified, or strengthened, as it is handed off from one enzyme to the next. Amplification would seem unlikely if the enzymes remain tethered to their scaffold proteins.

Now Carlos F. Lopez, Ph.D., Tina Iverson, Ph.D., Vsevolod Gurevich, Ph.D., and colleagues propose a "conveyor belt" mechanism for signal amplification by scaffold proteins, whereby an activated enzyme—in this case JNK3—is exchanged for an inactive enzyme on an arrestin-3 scaffold.

"This exchange is important biologically," they reported in the *Proceedings of the National Academy of Sciences*, as "formation of a tight complex would prevent the release of the downstream activated JNK3 and inhibit physiological response."

More information: Nicole A. Perry et al. Arrestin-3 scaffolding of the JNK3 cascade suggests a mechanism for signal amplification, *Proceedings of the National Academy of Sciences* (2018). DOI: 10.1073/pnas.1819230116

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