Macho muscle cells force their way to fusion

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In fact, according to new research from Johns Hopkins, the fusion of muscle cells is a power struggle that involves a smaller mobile antagonist that points at, pokes and finally pushes into its larger, stationary partner using a newly identified finger-like projection.

In a report published Nov. 29 in the Journal of Cell Biology, the researchers described experiments using fruit fly embryos to identify an invasive projection propelled by the rapid elongation of actin filaments as the main player in the cellular power struggle.

"We found that two muscle cells don't simply open up their membranes and symmetrically fuse together," says Elizabeth H. Chen, Ph.D., an assistant professor in the department of molecular biology and genetics, Johns Hopkins University School of Medicine. "Muscle cell fusion is actually an invasive battle."

Before the new study, it was assumed that actin-enriched blobs sit atop the membranes of muscle cells preparing to fuse, equally dispersed. But by observing the accumulation of these blobs by genetics means, the team concluded that the actin structure is produced in only one of the two muscle cell types — the aggressive fusion-competent myoblast — and not in the stationary founder cell. Further analyses of the images, made with an electron microscope, showed the myoblast is extending multiple finger-like protrusions toward founder cells and ultimately forcing fusion with the founder cell by forming an open pore.

"Where we once saw only blobs of actin, now we could clearly see finger-

like protrusions emanating from one cell into another," Chen says. "That really helped us make the connection between this structure and invasive podosomes."

The new work shows what is believed to be the first time that an invasive podosome-like structure has been found in developing tissue of any kind, Chen says, noting that although podosomes were discovered several decades ago in studies of cells growing in dishes, they have not been seen in a developing animal or implicated as a mechanism in cell fusion.

"It may be that this new understanding of muscle cell fusion will apply generally to other cells that fuse," Chen says, "such as egg and sperm, for instance, as well as bone resorption cells and cells that are vital for immune responses."

Muscle fusion is an integral part of muscle regeneration in genetic and acquired muscle diseases, and an accurate understanding of this basic cellular event could have important clinical applications in people with muscular dystrophy and other degenerative disorders, according to Chen.

More information: *Journal of Cell Biology*: jcb.rupress.org/

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