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Mayo Clinic

Mayo researchers describe measles viral protein movement

ROCHESTER, Minn. -- Mayo Clinic researchers have shown that proteins on the surface of a cell twist a viral protein into position, allowing the virus to start infection and cause disease, all in a movement as graceful as a ballroom dance. The findings appear in the current online issue of *Nature Structural & Molecular Biology*.

A team led by Roberto Cattaneo, Ph.D., a Mayo molecular biologist, describes the crucial initial steps taken by attachment proteins of the measles virus and related respiratory viruses with their cellular partners, the receptors. To get there, the research team built "handles" at different locations on a viral attachment protein, allowing them to be grabbed by an artificial receptor to start the dance.

Visualize the measles virus. It is small and has an outer "envelope" with two proteins, one that interacts with a cellular receptor, its dance partner, and another that fuses the viral envelope with the cell membrane, starting infection.

Measles virus, while long targeted for eradication through vaccination, still affects 10 million people and kills some 197,000 each year around the world. A long-running question is how the cell entry process begins.

"It was known that the viral attachment proteins always come in pairs, and recently it became clear that two pairs form a quartet," Dr. Cattaneo says. "Pairs initially face each other, and we show here that the upper bodies separate when the dance begins. We suggest that they then engage a partner from the other pair of the quartet, while the legs are still dancing with those of the original partner."

As this dance continues, the cellular receptors weaken the layer of attachment proteins that protects a lower layer of fusion proteins. When enough quartets become twisted and unstable, the top layer fails abruptly. This failure causes unfolding of the proteins in the lower layer, and, in turn, fusion with the cellular membrane. The viral genome, now inside the cell, tells it to stop dividing and mandates the building of new viruses.

Dr. Cattaneo has studied viruses for three decades, primarily as tools for new medical discoveries. Viruses, he says, can be transformed into vectors to treat disease. In 1999, he joined Mayo Clinic as a founding member of the Molecular Medicine Department. To date, two viral vectors developed at Mayo Clinic are in clinical trials to treat ovarian cancer, glioma and myeloma.

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Others on the team are Chanakha Navaratnarajah, Ph.D.; Levi Rupp; Leah Kay; and Vincent Leonard Ph.D., all of Mayo Clinic; and Numan Oezguen, Ph.D., and Werner Braun, Ph.D., from the University of Texas Medical Branch, Galveston. The research was supported by the National Institutes of Health and the Mayo Clinic Cancer Center.

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