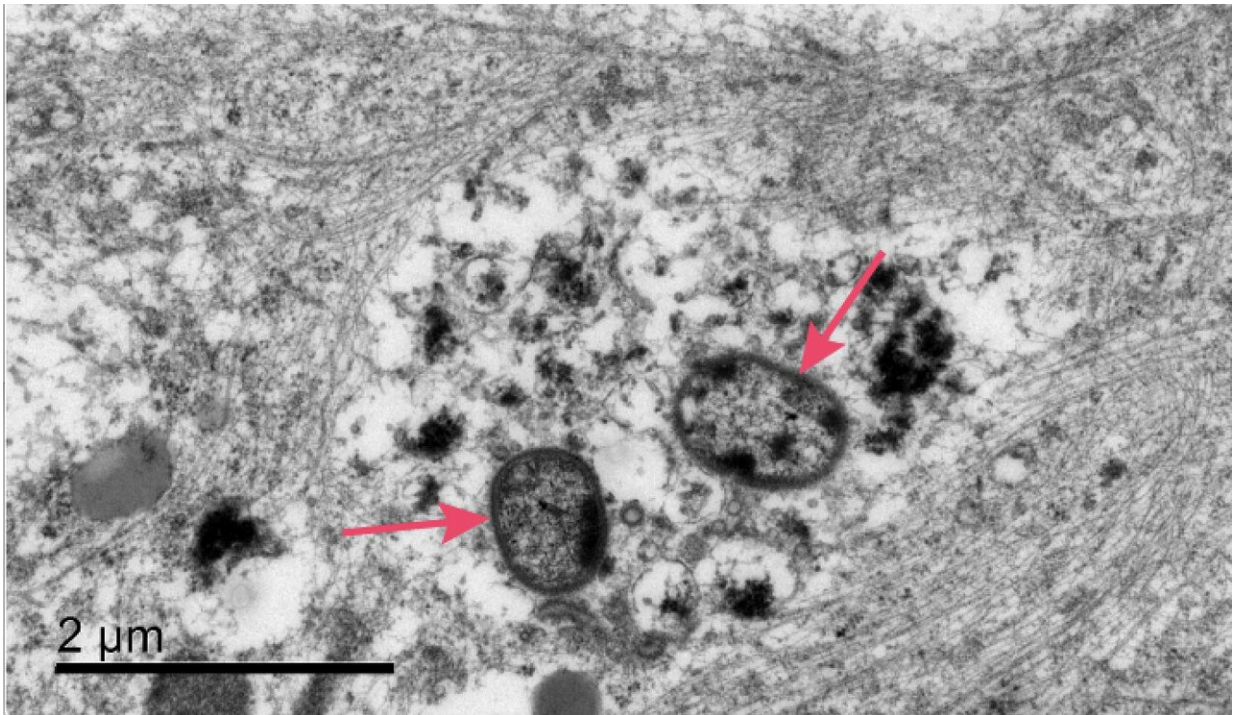


Cortexyme publishes data on *P. gingivalis* ability to infect neurons

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P. gingivalis bacteria (arrows), after invading a neuron, causes damage to the cellular infrastructure and synapses. Credit: Cortexyme, Inc.

Cortexyme, Inc., a clinical stage biopharmaceutical company pioneering a novel, disease-modifying therapeutic approach to treat what it believes to be a key underlying cause of Alzheimer's (AD) and other degenerative diseases, today announced the publication of research further

documenting the ability of the pathogen *Porphyromonas gingivalis* to invade neurons and trigger Alzheimer's-like neuropathology. The findings are to be published in the June 2020 issue of the *Journal of Alzheimer's Disease*; an early online version of the paper is available now so that the important findings can be rapidly disseminated to the research community.

"*P. gingivalis* is best known for its role as a primary driver of chronic periodontal disease, but researchers at Cortexyme and independent labs around the world have assembled a compelling body of data on its ability to infiltrate the brain and cause pathology characteristic of Alzheimer's disease," said Stephen Dominy, M.D., Cortexyme's chief scientific officer and co-founder, and co-author on the paper. "This latest research strengthens the connection between *P. gingivalis* and Alzheimer's, and underscores the importance both of studying the pathogen and targeting it with potential therapeutics, such as COR388."

As a Gram-negative, asaccharolytic bacterium, *P. gingivalis* breaks down proteins for its primary source of energy by utilizing toxic virulence factor proteases known as gingipains. Previous research led by the team at Cortexyme has demonstrated the presence of gingipains in greater than 90% of post-mortem brains of patients with AD. Cortexyme and others have also shown in animal models that *P. gingivalis* results in brain infection and classic AD pathology, including neurodegeneration, inflammation, beta-amyloid and tau pathology.

In the *JAD* paper available today, researchers demonstrate for the first time in vitro that *P. gingivalis* can invade and persist in mature human neurons expressing active gingipains, and that these *P. gingivalis*-infected neurons display signs of Alzheimer's-like neuropathology, including:

- disruption of the cytoskeleton, which is critical for proper

cellular function

- degradation of tau protein and increased tau phosphorylation, a key regulator of axonal transport mechanisms
- accumulation of intraneuronal autophagic vacuoles and multivesicular bodies, suggestive of disruption of normal lysosomal function
- synapse loss, one of the earliest pathological events in the onset of AD

"This research sheds new light on the ability of *P. gingivalis* to persistently infect and trigger Alzheimer's-like pathology in human neurons, providing additional evidence for the gingipain hypothesis of Alzheimer's causation that Cortexyme and our fellow researchers are aggressively pursuing," said Casey Lynch, chief executive officer, chair, and co-founder of Cortexyme. "We believe gingipain inhibition has the potential to be an important, differentiated mechanism of action against AD, and are committed to fully evaluating its potential in the GAIN Trial, the ongoing Phase 2/3 clinical study of COR388, our lead investigational medicine, in mild to moderate Alzheimer's disease."

More information: Ursula Haditsch et al, Alzheimer's Disease-Like Neurodegeneration in Porphyromonas gingivalis Infected Neurons with Persistent Expression of Active Gingipains, *Journal of Alzheimer's Disease* (2020). [DOI: 10.3233/JAD-200393](https://doi.org/10.3233/JAD-200393)

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