

BiophysTO Lunchtime Seminar Series

Date

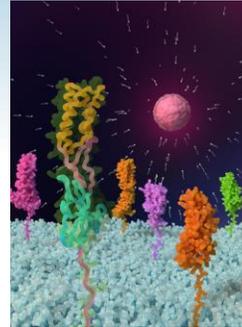
Thursday, Dec. 15th 2022
12:00 – 1:00 pm

Host: James Otis

Tyler Vance, Ph.D

Laboratory Medicine and Pathobiology
University of Toronto

Structure-function analysis of SPACA6: assembling the proteinaceous pieces of gamete fusion



The molecular machinery behind sperm-egg fusion in humans remains an unsolved puzzle; we have many of the pieces but do not know how they fit together. SPACA6 – a sperm-expressed surface protein – is one such piece. Despite being critical for gamete fusion during mammalian sexual reproduction, little is known about how SPACA6 specifically functions. We elucidated the crystal structure of the SPACA6 ectodomain at 2.2-Å resolution, revealing a two-domain protein containing a four-helix bundle and Ig-like β -sandwich. Using a combination of SAXS and H-DXMS, we were able to show that the linker between these two domains is flexible, allowing for alterations to the inter-domain orientation. SPACA6's structure is reminiscent of IZUMO1, another gamete fusion-associated protein, making SPACA6 and IZUMO1 founding members of a superfamily of fertilization-associated proteins, herein dubbed the IST superfamily. The IST superfamily is defined structurally by its distorted four-helix bundle and a pair of disulfide-bonded CXXC motifs. A structure-based search of the AlphaFold human proteome identified more protein members to this superfamily; remarkably, many of these proteins are linked to gamete fusion. The SPACA6 structure and its connection to other IST-superfamily members provide a missing connection in our knowledge of mammalian gamete-fusion puzzle.

Zoom Link: <https://utoronto.zoom.us/j/81725115773>

Meeting ID: 817 2511 5773



Seminar
Sponsors

UTSG

Biochemistry

Physics

Chemistry