

# JHU BIOLOGY DEPARTMENT SPECIAL SEMINAR

## Membrane Fusion in Mammalian Fertilization

**Guest Speaker**

**Steven Tang**

Department of Biochemistry, Stanford University School of Medicine

Host: John Kim

### Abstract:

Membrane fusion of sperm and eggs is pivotal in life. Understanding the molecular intricacies leading to sperm-egg fusion represents a basic science question with broad implications for human fertility and reproductive health. Despite substantial efforts, but how sperm and eggs bind to and fuse with one another has been largely undefined. Tmem95 (transmembrane protein 95) encodes a sperm acrosomal membrane protein, whose knockout has a male-specific sterility phenotype in mice. Tmem95 knockout murine sperm can bind to, but do not fuse with, eggs. How TMEM95 plays a role in membrane fusion of sperm and eggs has remained elusive. We utilized a sperm penetration assay as a model system to investigate the function of human TMEM95. We showed that human TMEM95 binds to hamster egg membranes, providing evidence for a TMEM95 receptor on eggs. Using X-ray crystallography, we reveal an evolutionarily conserved, positively charged region of TMEM95 as a putative receptor-binding surface. Amino acid substitutions within this region of TMEM95 ablate egg-binding activity. We identified monoclonal antibodies against TMEM95 that reduce the number of human sperm fused with hamster eggs in sperm penetration assays. Strikingly, these antibodies do not block binding of sperm to eggs. Taken together, these results provide strong evidence for a specific, receptor-mediated interaction of sperm TMEM95 with eggs and inform strategies for the identification of this egg receptor. We propose that this interaction has a direct role in facilitating sperm-egg fusion during fertilization.



**Tuesday, December 13th, 2022**  
**4pm - Mudd 100**