

Summary

The PhD project aims to decipher the physico-chemical mechanisms of successful fertilization of a mammalian egg - by a single sperm - and subsequent sperm neutralization to avoid pathological polyspermy, using microfluidics technology. Up to date, those phenomena remain poorly understood due to the specificities of the gametes and their mode of interaction. The presence of so-called zona pellucida (ZP), a shell surrounding an egg, becomes a barrier for sperm to reach the egg, while the large number and high motility of sperm penetrating the ZP render the identification of the fertilizing sperm and the site of sperm-egg membrane interaction unpredictable. As a result, conventional *in vitro* insemination is incompatible with the tracking of individual sperm with accurate spatiotemporal imaging of the molecular events underlying gamete fusion and polyspermy prevention. Despite the difficulties, we have recently identified two important cues: (i) a certain sperm head movement restricted by the ZP against the egg plasma membrane is essential for fertilization, and (ii) the release of egg-derived membrane vesicles into perivitelline space (PVS) in the ZP may turn sperm from a fusion-permissive to a fusion-inhibitory state after fertilization (PVS block). To quantitatively prove those important discoveries, we will develop microfluidic devices as powerful tools that allow us (i) to control the timing and location at which a sperm reaches the egg plasma membrane while immobilizing the egg to enable spatiotemporal imaging of the interaction site, (ii) to constrain sperm head movement against the egg plasma membrane by trapping the flagellum mimicking the effect of the ZP, (iii) to study the membrane rearrangements leading to fusion, (iv) to expose a sperm to PVS from a fertilized or unfertilized egg prior to the interaction with a ZP-free unfertilized egg, and (v) to decipher the molecular basis and kinetics of the PVS block.