Human Sperm Interactome network

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From a biological point of view, it is known that mammalian spermatozoa after ejaculation are unable to fertilize the oocyte. They need, to acquire the ability of fertilizing, to reside from hours to days within the female genital tract. Here, they interact with different molecules before to recognize and bind the oocyte. It is possible to define the Sperm–Egg Recognition and Binding as a multistep multi-molecular event, which involves not only the gametes but, virtually, all the female genital tract[1]. This strengthens the importance of an integrated approach in the study of reproductive medicine, with major references to male infertility. Often, the most common diagnostic and therapeutic approaches are not effective in treating infertility. The personalized medicine could address these challenges, by characterizing individuals' phenotypes and genotypes. Integration of biological knowledge and the personalized medicine are the prerequisite to realize a model able to represent the molecular interaction that characterize sperm physiology. We realized the Human Sperm Interactome Network 3.0 (HSIN3.0) starting from the pathway active in male germ cells.
The HSIN3.0 Interactome was built by a multistep approach. As first, we collected data from papers indexed in PubMed referred to Human Sperm Proteome or proteomic studies of sperm biology. Then, staring from the list of identified proteins, we carried out a network enrichment and pathways reconstruction analysis through Reactome FI; Pathway Commons and String. Quality control and network creation was performed by some ad-hoc implemented Python scripts. Finally, with Cytoscape 3.4.0 was used to realize the network[2]. All the analysis have been carried out with the plug-in Network Analyzer (http://apps.cytoscape.org/apps/networkanalyzer).
The HSIN3.0 is constituted by 7891 nodes linked by 14712 links, and 25 connected components. In particular, we identified a Main Connected Component (HSNI3.0_MC) that accounts for 7758 nodes and 14534 links. The analysis of HSNI3.0_MC showed that it is characterized by a scale free topology that follows the Barabasi-Albert (BA) model but with a tendency to develop hierarchical pattern. The number of links per node (the node degree) follows a power law, with a negative exponent ($y = a\ x^{-1.764}$, $R2 = 0.771$), and the clustering coefficient (cc), which is a measure of the network tendency to form clusters, is low ($cc = 0.140$). In addition, HSNI3.0_MC is characterized by an ultra-small world topology: the averaged of. neighbours, which represents the mean number of connection of each node, is 3.746 and the characteristic path length, which gives the expected distance between two connected nodes, is 7.413.
These specific features, scale-free and ultra-small world architecture, describe a network resistant to random attacks and that is designed to respond quickly and specifically to external inputs. In addition, it has been possible to identify the most connected nodes (the hubs) and bottlenecks nodes. These results allowed us to explore the control mechanisms that drives sperm biochemical machinery and to verify different levels of control. Finally, we found that several key-nodes representing molecules specifically involved in function that are usually considered as not present or not active in sperm cells, such as control of cell cycle, proteins synthesis, nuclear trafficking, and immune response.
These approach could be helpful to identify new perspectives in the study of sperm biology and to identify potential diagnostic markers concurring in explaining male "idiopathic infertility", which are, at the present, one of the most important causes of fertilization failure.

1. Bernabò et al OMICS. 2014, 18(12):740-53
2. Bernabò et al., BMC Syst Biol. 2010, 4:87.

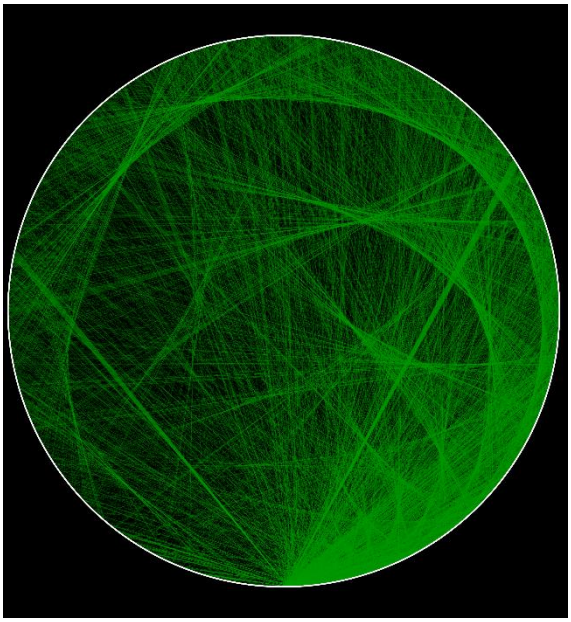

Figure 1. Network representing HSIN3.0 Interactome in spermatozoa

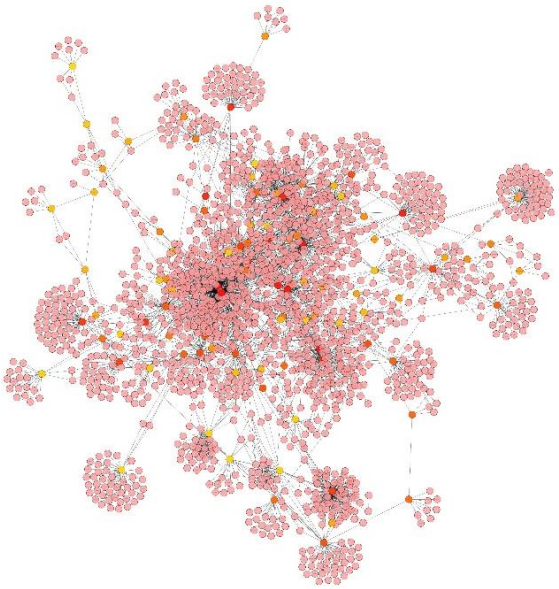

Figure 2. Network representing Bottleneck with the first-stage nodes

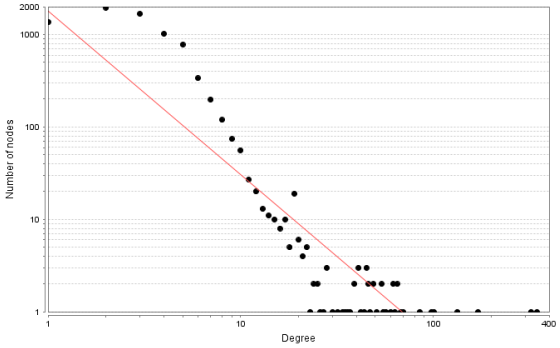

Figure 3. Node Degree Distribution

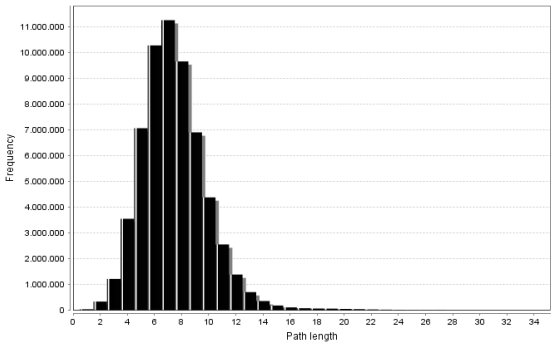

Figure 4. Shortest Path Length Distribution