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SIGNALING PATHWAYS IDENTIFIED BY SYSTEMS ANALYSIS OF *LEISHMANIA* DIFFERENTIATION

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During their life, *Leishmania* cycle between phagolysosomes of mammalian macrophages and the sand fly mid-gut, proliferating as intracellular amastigotes and extracellular promastigotes, respectively. While much of the molecular mechanism of development inside macrophages remains a mystery, development of a host-free system that simulates phagolysosome conditions (37 ºC and pH 5.5, 5% CO_2) has provided new insight into these processes. Time course transcriptomic and proteomic analyses indicated that differentiation is a coordinated process that results in adaptation to life inside phagolysosomes. Quantitative phosphoproteomics revealed extensive differences in phosphorylation between promastigotes and amastigotes, and identified stage-specific phosphorylation motifs. The analyses revealed protein kinases that phosphorylate specifically by the differentiation signal at the beginning of differentiation, but not by either high temperature or acidic pH alone. Null mutants of early activated protein kinases revealed a role for protein kinase A (PKA) in differentiation initiation. All in all, our work pioneered the first insight into the molecular mechanism of *Leishmania* differentiation and identified the signaling pathway that initiates *Leishmania* promastigote to amastigote differentiation.

Biography

Dan Zilberstein graduated in Microbiology at the Hebrew University of Jerusalem, then a post doctorate in molecular parasitology at the U.S. National Institutes of Health. In 1986 he started his own laboratory at the Faculty of Biology at the Technion-Israel Institute of Technology. He became professor on 1994 and between 2001 and 2006 he was the Dean of the Faculty of Biology. In 2012 he became member of Technion council and head of Tehnion pre-university education center. To date, Dr. Zilberstein published over 80 peer review papers, reviews and book chapters. Thirty five students graduated under his supevision.

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