POSTERS

FROM SIGNALING TO STRUCTURE: TYPE 1 DIABETES DISRUPTS ACTIN NETWORKS IN TESTIS AND SPERMATOZOA

A. Biasi[1], M. R. Ambruosi[1], S. Falvo[2], S. Minucci[1], M. Venditti[1]

[1]Dept of Experimental Medicine, University of Campania "L. Vanvitelli"; [2]Dept. of Environmental Biological and Pharmaceutical Sciences and Technologies, University of Campania "L. Vanvitelli", Italy

Type 1 diabetes (T1D) is a systemic metabolic disorder that affects not only glucose homeostasis but also the physiology of the male reproductive system. In particular, alterations in cytoskeletal organization have emerged as a key determinant of impaired spermatogenesis. This study investigated the impact of T1D on actin cytoskeleton dynamics and its regulatory networks in rat testis and spermatozoa (SPZ).

T1D was induced in adult Wistar rats by i.p. administration of streptozotocin (65 mg/kg). Analysis of testicular tissue revealed marked alterations in F-actin organization, indicating a profound disruption of cytoskeletal architecture. To further characterize the molecular mechanisms underlying these changes, key regulators of actin dynamics were evaluated. T1D significantly affected the expression of actin-associated proteins involved in filament capping and bundling (EPS8, Fascin), as well as actin nucleation and branching (N-WASP, ARP2/3 complex), suggesting impaired control of filament organization.

Additionally, planar cell polarity signaling was dysregulated, with alterations in Frizzled receptors, Dishevelled phosphorylation, DAAM1, RhoA activation, and ROCK signaling. Consistently, downstream regulators of actin turnover were affected, as shown by altered LIMK1 and cofilin phosphorylation, supporting increased filament destabilization. In parallel, modulation of cytoskeleton-associated signaling pathways, including RICTOR, PKC, AKT, and MARCKS, further highlighted the broad impact of T1D on actin regulatory networks.

Finally, these alterations extended to SPZ, where changes in F-actin organization and DAAM1 localization were observed, suggesting a direct impact on sperm structure and function.

Overall, these findings demonstrate that T1D disrupts actin cytoskeleton dynamics at multiple regulatory levels, from upstream signaling pathways to structural effectors, ultimately contributing to impaired spermatogenesis and reduced sperm quality. These results identify actin-related pathways as potential targets for therapeutic intervention in diabetic male infertility.