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THE ROLE OF EXOSOMES IN EARLY DIAGNOSIS AND TREATMENT OF DIABETES MELLITUS

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Diabetes mellitus continues to pose a major global health challenge, with increasing incidence rates and ongoing difficulties in maintaining effective glycemic control without triggering side effects such as hypoglycemia, weight gain, and cardiovascular events. At present, the main treatment options include oral antidiabetic drugs and external insulin delivery. These approaches offer only temporary blood glucose regulation and neither reverse the disease nor halt its long-term complications.

The objective is to explore the diverse functions of exosomes as both early biomarkers for diagnosis and therapeutic tools in diabetes and its associated complications.

Exosomes are tiny vesicles released by cells into their external environment. Various chemical and physical stimuli—such as inflammatory cytokines, non-esterified cholesterol, thrombin, tobacco smoke extract, low oxygen tension (hypoxia), and mechanical shear forces—can activate cells or induce apoptosis. Such activation leads to inward budding of the endosomal membrane and the formation of multivesicular bodies (MVBs). These MVBs then fuse with the plasma membrane, releasing exosomes. Many cell types can produce exosomes, including tumor cells, stem cells, muscle cells (skeletal), mast cells, dendritic cells, and lymphocytes. Research on exosomes primarily focuses on their cargo: functional microRNAs, small amounts of messenger RNA, long non-coding RNAs (lncRNAs), specific proteins (e.g., cytokines and growth factors), and other biologically active molecules. The lipid bilayer inherited from the parent cell protects these molecules from enzymatic degradation. Thus, exosomes act as intercellular messengers that can modify recipient cell behavior through fusion, endocytosis, or ligand–receptor interactions.

Exosome composition differs between healthy individuals and those with diabetes, and these differences become more pronounced when diabetic complications arise. Protein content in exosomes isolated from diabetic patient's body fluids also changes significantly. One example is dipeptidyl peptidase-IV (DPP-IV), an enzyme that inactivates glucagon-like peptide-1 (GLP-1) and is associated with diabetes. In urine, microvesicles serve as the main carriers of DPP-IV, and their levels are notably elevated in type 2 diabetes patients compared to healthy controls. Moreover, urinary exosomal levels of Wilms tumor protein 1 are markedly higher in diabetic patients with proteinuria, suggesting that exosomes could serve as early markers of podocyte injury.

Additionally, altered microRNA expression has been observed in exosomes from diabetic individuals, regardless of whether complications have developed. Because these exosomal biomarkers change before tissue damage becomes apparent and offer greater precision than whole-blood or urine markers, they hold significant potential for the early detection of diabetes and its complications. Exosomes derived from human endothelial progenitor cells carry pro-angiogenic factors—including FGF-1, VEGFA, VEGFR-2, ANG-1, E-selectin, CXCL-16, eNOS, and IL-8—and accelerate wound healing in diabetic rats by enhancing endothelial cell proliferation, migration, and tube formation via the Erk1/2 signaling pathway.

These findings suggest that endogenous exosomes in diabetic patients are functionally impaired and fail to properly regulate cell-to-cell communication, whereas externally administered exosomes might correct this dysfunction. Consequently, exosomes are promising not only as early diagnostic biomarkers for diabetes mellitus but also as novel therapeutic agents for the disease and its complications.