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Directed-Exosome Mediated Gene, Delivered as mRNA, Therapy – A Generic Approach for Cancer and Other Treatments

A. C. Matin
Stanford University School of Medicine, USA

Exosomes, being nature's own antigen delivery vehicles, are ideal for gene delivery. Here, treatment of HER2+ breast cancer (BC) by prodrugs [CNOB or CB1954 (aka tretazicar)] is described. Prodrugs are harmless until activated by a bacterial or viral gene-encoded enzyme (e.g., HChrR6); if gene delivery is confined to the cancer, treatment can be without side-effects of conventional chemotherapy. mRNA is superior to DNA for gene delivery: it is translated directly upon cytosol entry and its expression is higher and lasts longer, which is important, as short-lived expression has constrained gene therapy. We loaded the exosomes with HChrR6 mRNA, using a plasmid, and later to improve safety, directly; this had not been done before. The loaded exosomes were incubated with our "EVHB" protein, which exhibits anti-HER2 scFv antibody and is capable of tethering to the exosomes by its lactadherin C1-C2 domains, making them specifically target HER2+ BC. Systemic delivery of these exosomes and either of the prodrug completely arrested HER2+ BC xenograft growth in athymic mice – no other organ was injured. We posit that recruiting immunity will result in complete cure: tumor ablation evokes strong anti-tumor immune response; and as the exosomes target the tumor, any immune response against them will bolster tumor killing. This is being tested in immunocompetent mice, which spontaneously develop HER2+ BC. The anti-HER2 scFv in the EVHB protein can be replaced by scFvs able to target other receptors/ligands. Thus, this approach is generic and can treat any disease overexpressing a marker, which applies to many ailments.

Biography:

A. C. Matin has been a full professor at Stanford University for several years and is affiliated with several programs, including the Stanford Cancer Research Institute. He has contributed too many areas of biological research, including bacterial infections and their treatment; discovery of new drugs and therapeutic enzymes and their improvement; as well as their specific targeting to cancer (and other diseases). He did his Ph. D. at UCLA, spent some years in the Netherlands (State University of Groningen), where he directed a research group, before joining Stanford. He is recipient of numerous awards and honors.