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Design of dendrimer-based drug delivery nanodevices with enhanced therapeutic efficacies[1]

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Dendrimers and hyperbranched polymers possess highly branched architectures, with a large number of controllable, tailorable, 'peripheral' functionalities. Since the surface chemistry of these materials can be modified with relative ease, these materials have tremendous potential in targeted drug delivery. They have significant potential compared to liposomes and nanoparticles, because of the reduced macrophage update, increased cellular transport, and the ability to modulate the local environment through functional groups. We are developing nanodevices based on dendritic systems for drug delivery, that contain a high drug payload, ligands, and imaging agents, resulting in 'smart' drug delivery devices that can target, deliver, and signal. In collaboration with the Children's Hospital of Michigan, Karmanos Cancer Institute, and College of Pharmacy, we are testing the *in vitro* and *in vivo* response of these nanodevices, by adapting the chemistry for specific clinical applications such as asthma and cancer. These materials are characterized by UV/Vis spectroscopy, flow cytometry, fluorescence/confocal microscopy, and appropriate animal models. Our results suggest that: (1) We can prepare drug-dendrimer conjugates with drug payloads of greater than 50%, for a variety of drugs; (2) The dendritic polymers are capable of transporting and delivering drugs into cells faster than free drugs, with superior therapeutic efficiency. This can be modulated by the surface functionality of the dendrimer; (3) For chemotherapy drugs, the conjugates are a factor of 6-20 times more effective even in drug-resistant cell lines; (4) For corticosteroidal drugs, the dendritic polymers provide higher drug residence times in the lung, allowing for passive targeting. The ability of the drug-dendrimer-ligand conjugates to target specific asthma and cancer cells is currently being explored using *in vitro* and *in vivo* animal models.

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