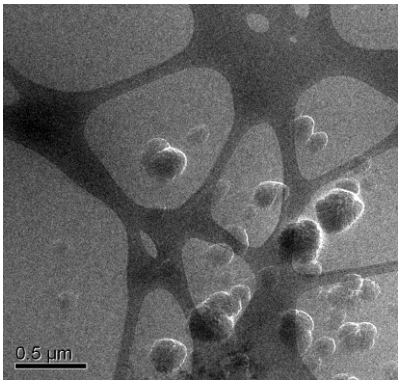
Smadar Cohen - Research Abstract

The Cohen group is developing targeted nanoparticulates (NPs) for controlled drug delivery and biomaterial scaffolds for tissue engineering and regenerative medicine, by applying advanced materials and tools, which are bio-inspired by nature. For example, we recently developed NPs with mono-disperse size and with controlled drug release properties by employing the principle of molecular self-assembly. NP formation has been driven by the affinity binding of alginate-sulfate, synthesized in our laboratory from the algae-derived alginate, and positively-charged molecules, while creating mono-dispersed (100 nm diameter) NPs, under aqueous conditions (1,2). The feasibility of these unique NPs to sustain drug release was proven *in vitro* and *in vivo* (3, 4). These unique NPs have additional advantages; 1) the simple preparation method at aqueous conditions ("green technology") is important for NP scalable production; 2) the NPs have functional carboxylates, so that targeting moieties (peptides, antibodies, receptors) can be attached onto their surface for the purpose of their targeting to cells/organs and enhancing NP penetration into cells; and 3) the relative negative surface charge makes these NPs bio-compatible, nontoxic and less amenable to opsonization and removal from circulation.

We now address the cell uptake, internalization and intracellular localization of these unique NPs, as a function of their size, surface charge and the presence of surface-attached targeting ligands. Our long term goal is to gain sufficient understand to enable NPs design, enabling their efficient localization in the cytosol- the site of action of many molecules including siRNA molecules.



Cryogenic TEM picture of NPs formed due to affinity interactions between alginate-sulfate and hepatocyte growth factor (Ruvinov *et al*, In Preparation)

References:

1. Freeman I, Kedem A, Cohen S. (2008) The effect of sulfation of alginate hydrogels on the specific binding and controlled release of heparin-binding proteins. Biomaterials, 29: 3260-68.
2. Freeman I, Cohen S. (2009) The influence of sequential delivery of angiogenic factors from affinity binding alginate scaffolds on vascularization. Biomaterials, 30: 2122–31.
3. Ruvinov E, Leor J, Cohen S. (2010) Controlled HGF delivery from an affinity-binding alginate biomaterial induces angiogenesis and improves perfusion in a hindlimb ischemia model. Biomaterials, 31: 4573-82.
4. Ruvinov E, Leor J, Cohen S. (2011) Sequential delivery of IGF-1 and HGF promotes myocardial repair after myocardial infarction. Biomaterials, 32: 565-578