Injectable, Tough Alginate Cryogels as Cancer Vaccines

Ting-Yu Shih[1,2], Serena Blacklow[1], Weiwei Aileen Li[1,2], Sidi Bencherif[1,2], Sandeep Koshy[1,2,3], David J Mooney[1,2]

[1]School of Engineering and Applied Sciences, Harvard University;

[2]Wyss Institute for Biologically Inspired Engineering at Harvard University;

[3]Harvard-MIT Division of Health Sciences and Technology

Category: Immunotherapy, Bioengineering

Cancer vaccines have the potential to eliminate tumors and prevent recurrence. Recently, a covalently crosslinked methacrylated (MA)-alginate cryogel-based vaccine has been shown to successfully modulate host immune cells *in situ* and evoke potent antitumor responses. The cryogel allows minimally invasive delivery but is not mechanically robust and requires a large 16G needle for delivery. A network of covalently and ionically crosslinked polymers has previously demonstrated strikingly high toughness in bulk form. Therefore, we hypothesized that combining covalent and ionic crosslinking would result in a tough MA-alginate cryogel with improved injectability.

Cryogels were fabricated by covalently crosslinking MA-alginate by free radical polymerization at -20°C overnight. The cryogels were then soaked in a calcium chloride solution to introduce ionic crosslinking. The cryogels were injected through a 16G needle repeatedly until visible damage was observed. Increasing calcium concentration in the cryogel led to enhanced injectability up to 37 mM, beyond which injectability decreased. The optimized tough cryogels could be injected via an 18G needle while maintaining their gel structure; all of the covalently crosslinked only cryogels fractured when injected through this needle size. The tough cryogel provided sustained release of the dendritic cell (DC) chemoattractant GM-CSF and adjuvant CpG-ODN *in vitro*. Tough cryogels delivering GM-CSF recruited five times more DCs than blank gels by Day 7 *in vivo*. The tough cryogel vaccine with irradiated HER2+ breast cancer cells as antigen generated significantly higher anti-HER2 antibody titer than blank gels and provided complete protection against breast cancer in 60% of the mice for at least 7 weeks in a prophylactic vaccination study. These tough cryogels provide a promising minimally invasive delivery platform for cancer vaccinations.