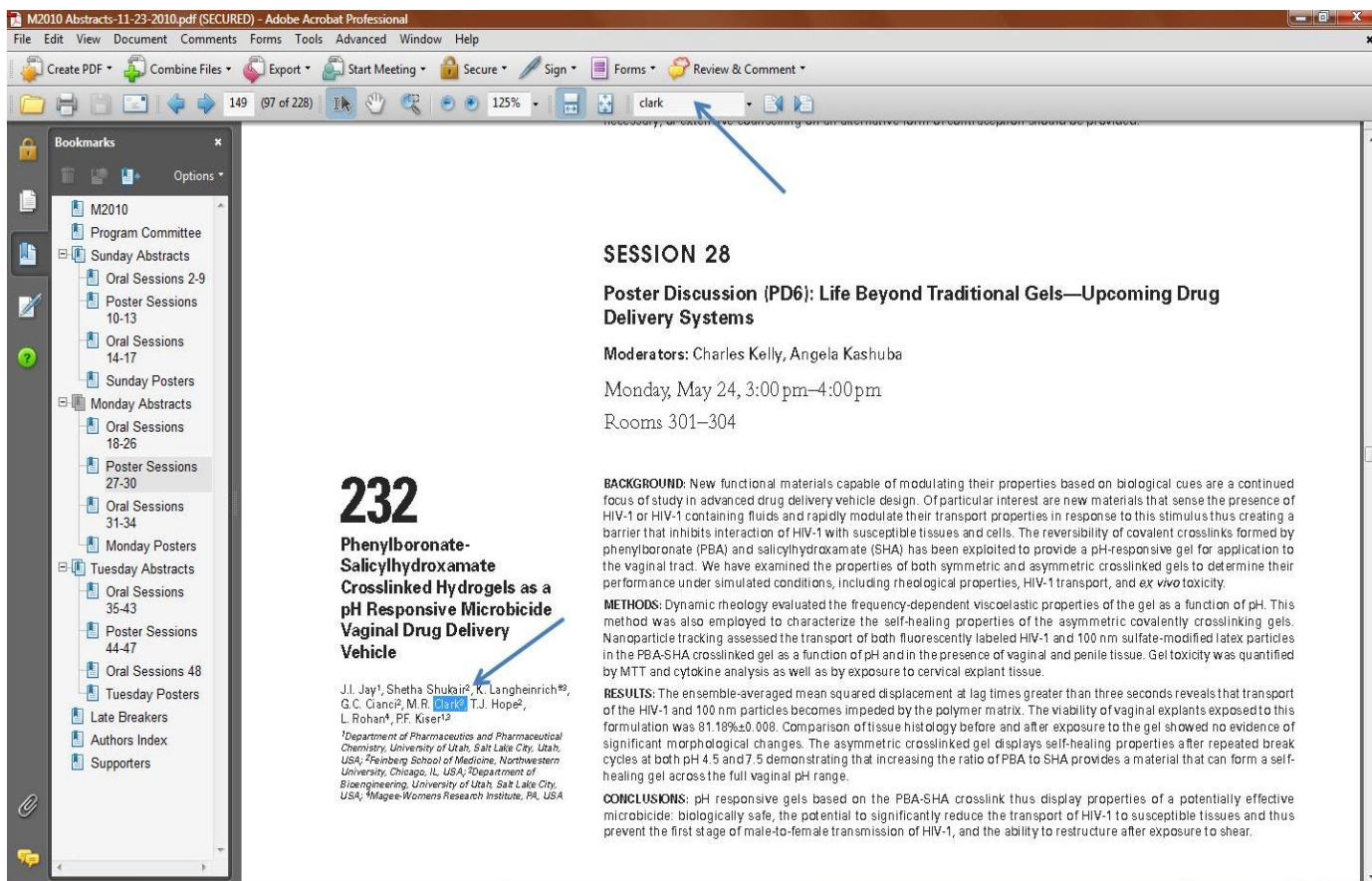


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**SESSION 28**  
**Poster Discussion (PD6): Life Beyond Traditional Gels—Upcoming Drug Delivery Systems**  
Moderators: Charles Kelly, Angela Kashuba  
Monday, May 24, 3:00 pm–4:00 pm  
Rooms 301–304

**232**  
**Phenylboronate-Salicylhydroxamate Crosslinked Hydrogels as a pH Responsive Microbicide Vaginal Drug Delivery Vehicle**  
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**BACKGROUND:** New functional materials capable of modulating their properties based on biological cues are a continued focus of study in advanced drug delivery vehicle design. Of particular interest are new materials that sense the presence of HIV-1 or HIV-1 containing fluids and rapidly modulate their transport properties in response to this stimulus thus creating a barrier that inhibits interaction of HIV-1 with susceptible tissues and cells. The reversibility of covalent crosslinks formed by phenylboronate (PBA) and salicylhydroxamate (SHA) has been exploited to provide a pH-responsive gel for application to the vaginal tract. We have examined the properties of both symmetric and asymmetric crosslinked gels to determine their performance under simulated conditions, including rheological properties, HIV-1 transport, and *ex vivo* toxicity.

**METHODS:** Dynamic rheology evaluated the frequency-dependent viscoelastic properties of the gel as a function of pH. This method was also employed to characterize the self-healing properties of the asymmetric covalently crosslinking gels. Nanoparticle tracking assessed the transport of both fluorescently labeled HIV-1 and 100 nm sulfate-modified latex particles in the PBA-SHA crosslinked gel as a function of pH and in the presence of vaginal and penile tissue. Gel toxicity was quantified by MTT and cytokine analysis as well as by exposure to cervical explant tissue.

**RESULTS:** The ensemble-averaged mean squared displacement at lag times greater than three seconds reveals that transport of the HIV-1 and 100 nm particles becomes impeded by the polymer matrix. The viability of vaginal explants exposed to this formulation was 81.18%±0.008. Comparison of tissue histology before and after exposure to the gel showed no evidence of significant morphological changes. The asymmetric crosslinked gel displays self-healing properties after repeated break cycles at both pH 4.5 and 7.5 demonstrating that increasing the ratio of PBA to SHA provides a material that can form a self-healing gel across the full vaginal pH range.

**CONCLUSIONS:** pH responsive gels based on the PBA-SHA crosslink thus display properties of a potentially effective microbicide: biologically safe, the potential to significantly reduce the transport of HIV-1 to susceptible tissues and thus prevent the first stage of male-to-female transmission of HIV-1, and the ability to restructure after exposure to shear.