Oncolytic virotherapy is the use of live virus vectors to treat cancer by selectively infecting and killing cancerous cells, while sparing normal cells and tissues. Oncolytic viruses (OVs) are often modified genetically to improve the selectivity of cancer cell tropism and/or induce an exacerbated anti-tumor immune response and can be used in conjunction with other cancer therapies, particularly immune checkpoint inhibitor antibodies. The McFadden lab is devoted to the study of a poxvirus called myxoma virus (MYXV) for cancer therapy and this has led to a new ASU spinoff company called OncoMyx that is devoted to the development of human clinical trials using multi-armed oncolytic MYXV. As an example, one cancer target for oncolytic MYXV is multiple myeloma (MM), a hematologic cancer of bone marrow derived plasma cells. In a recent paper (Villa et al, Mol Therapy-Oncolytics, in press), we have tested three related systemic strategies to deliver oncolytic myxoma virus to sites of MM in the bone marrow and spleen. The model exploited is a Balb/c immunocompetent mouse pre-seeded into the BM and spleen with dsRed-tagged syngeneic murine MM, and the MYXV delivery strategies tested were: 1- intravenous injection of free MYXV, 2- infusion of murine PBMCs pre-loaded ex vivo with MYXV, and 3- infusion of murine BM leukocytes pre-loaded ex vivo with MYXV. The last method is designed to mimic patients who receive autologous BM transplants as part of their therapeutic regimens. Although all three delivery strategies provided varying degrees of long-term clearance of the MM, there was a clear hierarchy of their anti-tumor efficacies. In collaboration with colleagues based at the Mayo Clinic in Scottsdale, we have also tested oncolytic MYXV against primary clinical specimens of human MM derived from samples from patients who have failed standard therapies. In general, these studies all affirm the potential for oncolytic virotherapy with MYXV as a new cancer therapy modality in the future.