

## *A Novel phage-based screening technology for antivirals*



**Principal Investigator:** Matthias Götte, McGill University

**Co-Investigator:** Guy Boivin (Université Laval)

Infection with herpesviruses is associated with important human diseases including the development of cancers. Temporal or permanent deficiencies in the immune system can facilitate infection with these viruses. Patients who receive organ transplants are considered to be the most vulnerable population. Ideally, those individuals are treated with antiviral agents to prevent infection.

Unfortunately, the use of approved drugs is often associated with severe side effects, the development of drug resistance, and a limited spectrum of activity against the various members of the herpesvirus family. Thus, there is an urgent medical need to discover and to develop novel anti-herpetic agents. However, technical obstacles have hampered the development of effective drugs against many of these viruses. Here we propose to develop a surrogate system that takes advantage of the structural and functional similarities among viral DNA polymerases and their orthologs in phages. The central hypothesis is that phage-derived chimeric polymerases containing critical parts of the substrate binding site of the viral enzyme can be used to identify novel classes of compounds that inhibit essential functions of the virus.

This novel technology has the potential to enable the discovery of small molecule drugs with broad antiviral activity against the various members of the herpesvirus family. The heart of the proposed research is that these compounds can be identified in bacteria, which will drastically reduce time and costs in the discovery process. Moreover, screening for these compounds in a biological environment, i.e. in bacteria, renders this assay potentially highly sensitive.

The principle of this technology could be translated to other viruses and, thus, address challenges in a broad range of therapeutic indications.