

## THE “BLOCKERS OF DISEASE-ASSOCIATED CONFORMATION” (DAC BLOCKERS) PLATFORM

The “Blockers of Disease-Associated Conformation” (DAC Blockers) platform is a new discovery platform for the identification of peptides that block proteins from adopting their disease-associated conformations. To date, two of the predicted therapeutic peptide candidates from the pilot validation run of the platform have shown initial experimental verification, one with anti-inflammatory and the other with anti-cancer activities.

The newly developed DAC Blockers platform has been designed to identify segments in proteins of interest that, if introduced therapeutically as synthetic peptides, would block specific conformational changes of such proteins, and thereby prevent them from adopting disease-associated conformations and related activities. A key capability of the platform is that it enables the proteome-wide search for such conformational change blocking peptides in human, viral and bacterial proteomes.

An initial run of the discovery platform resulted in the *in silico* prediction of therapeutic peptide candidates for approximately 40 drug targets of interest with potential usage for various indications, including solid cancers, inflammatory diseases, septic shock and viral diseases. Seven of these drug targets were selected for initial experimental validation and peptide blockers were found for all seven targets.

In addition, to date, two of these peptides have shown biological efficacy in experimental models, further demonstrating both their potential therapeutic utility and the validity of the platform’s predictive capability. For example, acute *in-vivo* administration of one of these peptides (CGEN-25007) was shown to significantly reduce the serum levels of inflammatory cytokines in mice treated with lipopolysaccharide. In other experimental models, the second peptide (CGEN-25008) was shown to induce growth arrest and enhance the susceptibility to chemotherapy agents in breast, lung and prostate cancer cell lines *in vitro* and *in vivo*. These peptides are currently undergoing further evaluation in disease-related animal models. Experimental testing is in the planning stages for additional peptide candidates discovered to date.