Glioblastoma is a highly aggressive form of brain cancer. Therapeutic intervention of glioblastoma through epigenetic shapers such as CHD4 is established as a promising avenue for clinical impact. Despite the accumulating evidence suggesting the importance of CHD4 in glioblastoma, little effort has been done to develop specific CHD4 inhibitors.

In his lab, Dr. Nurmemmedov and his team have taken a unique approach to targeting CHD4 in glioblastoma. They have designed a two-arm therapeutic discovery approach that combined tiling CRISPR screen together with rational chemical biology. The CRISPR study identified the therapeutically vulnerable sites of the CHD4 protein. On the other hand, using rigorous biology and chemistry, the team has identified several novel inhibitors of CHD4. They hypothesize that a selective CHD4 inhibitor would specifically impair tumor growth while sparing healthy cells and could potentially have a therapeutic application for glioblastoma. These inhibitors demonstrate selectivity, target engagement, and unique mechanism of action. Once fully investigated, these molecules could be used to prevent therapy resistance in glioblastomas, with potential translation to the clinic.