

Mohammad Aarif Siddiqui has received DKK 1.700.000 as a postdoctoral grant by Lundbeck Foundation for the project Targeting splicing for the chemo-prevention of brain metastases.

The project aims to develop a therapeutic strategy against brain metastasis by altering splicing of thymidylate synthase (TS) mRNA using **splice switching oligonucleotides (SSOs)**. Brain is one of the common metastasis sites, and there are fewer chemotherapy options in brain metastasis. Our preliminary experiments show that a class of molecules called SSOs could be used to reduce the level of a life essential enzyme, **thymidylate synthase (TS)**, by affecting pre-mRNA splicing and thereby reduce the growth of cancer cells. SSOs have the benefit of low toxicity, easy delivery and high stability in brain. Furthermore, SSOs have already been approved as drugs for several diseases.

Therefore, we will explore the use of SSOs targeting TS, not only as an option for treatment of in brain metastasis, but also as a strategy for metastasis prevention. Our project will be focused on lung- and colorectal-cancer because patients with these cancers are currently treated with enzymatic inhibitors of TS. The project could be paving a way to design similar strategies in other cancers.

