abstracts: poster presentations

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This expression system is particularly suited for synthesizing mRNA and protein in a coupled *invitro* transcription and translation system which represents an easy way for probing protein-protein interactions. Identifying robust protein binding partners for MAGE-B2 is key to ascribing a cellular function not only for this particular MAGE but also to the general MAGE family. We will then test validated binding partners for contribution to MAGE-B2's established tumorigenic, pro-proliferative effect by siRNA mediated transcript knockdown. A successful validation will require at least partial recapitulation of the MAGE-B2 depletion effects in cancer cells. Using this systematic approach, we aim to outline a mechanistic basis for MAGE-B2 function.

P1385

Biophysical investigation of p53(Y220C) mutant and its interaction with potent small molecule modulators

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Transcription factor p53 is an oncosuppressor protein that is activated in response to various types of cellular stress. In many cases p53 regulates the expression of genes whose protein products lead to cell cycle arrest and/or apoptosis. In addition, in about 50% of human cancers p53 tumor suppressor inactivation occurs as a result of point mutations, primarily in the DNA-binding domain. Oncogenic mutation Y220C is one of the most common for p53 and is detected annually in about ~100,000 diagnosed cancer cases. The presence of this mutation violates the tertiary structure of the DNA-binding domain p53, which leads to destabilization of the protein, its partial denaturation and loss of activity. Stabilization of the mutant p53(Y220C) structure and activation of its disturbed transcription functions is possible with the help of small molecules described in the literature as stabilizers, activators or modulators.The aim of this project is to study the interaction of derivatives of MB725, developed in collaboration with the team of Prof. Matthias Baud (University of Southampton, UK) with recombinant p53(wt) and p53(Y220C). Protein expression was carried out in the bacterial strain *E.coli* BL21(DE3)pLysS. Purification of protein was performed by metal-chelate affinity, ion-exchange and gel-filtration chromatography. Binding of the compounds to proteins was subsequently assessed biophysically using differential scanning fluorimetry (DSF), surface plasmon resonance (SPR) and isothermal titration calorimetry (ITC). Compounds showing high affinity for the mutant protein were selected for structural biology analysis by X-ray diffraction. At the moment, the optimization of conditions for growing crystals of the recombinant protein p53(Y220C) is being carried out. High quality crystals will be soaked with the most potent compounds. Diffraction data will be collected using Rigaku XtaLAB Synergy-S diffractometer with HyPix-6000NE hybrid photon counting detector.Further studies of the interaction of MB725 derivatives with the recombinant proteins p53(wt) and p53(Y220C) are important for the development of novel personalized anticancer drugs that target mutant proteins. The study was funded by RSF grant 19-74-10022 to EB. References Chasov V, Mirgayazova R, Zmievskaya E, Khadiullina R, Valiullina A, Stephenson Clarke JR, Rizvanov A, Baud MG, Bulatov E. Key players in the mutant p53 team: small molecules, gene editing, immunotherapy. Frontiers in Oncology. 2020; 10. DOI: 10.3389/fonc.2020.01460