Research profile for applicants

Name of DKFZ research division/group:	***Translational Control and Metabolism (B250)***
Contact person:	***Fabricio Loayza-Puch*** ***Email: f.loayza-puch@dkfz.de*** ***Phone: +49 6221 42 363***
Group homepage: *Visit this website for further information on current research and recent publications.*	***https://www.dkfz.de/en/translationskontrolle-stoffwechsel/index.php***
Eligibility:	• ***DKFZ Postdoctoral Fellowships***

RESEARCH PROFILE AND PROJECT TOPICS

The Loayza-Puch laboratory uses a combination of innovative sequencing techniques and functional genomics in order to understand the role of mRNA translation in cancer and metastasis. We are particularly interested in dissecting the role of regulatory elements in non-coding regions of mRNA. Our group also exploits the cellular translation machinery to uncover metabolic limitations in cancer (Loayza-Puch et al., 2016)

Project description.
Recent advances in neoantigen research have accelerated the development and regulatory approval of tumor immunotherapies. These therapies include cancer vaccines, adoptive cell therapy, and antibody-based treatments, particularly for solid tumors. Neoantigens are newly created antigens produced by tumor cells due to various tumor-specific changes, such as genomic mutations, dysregulated RNA splicing, abnormal post-translational modifications, and aberrant translation events.

Using ribosome profiling, our group found that in response to chemotherapy, breast cancer cells activate a non-canonical translational program. This results in aberrant protein synthesis and the expression of thousands of unannotated proteins derived from the 5' untranslated regions (UTR) of mRNAs. Notably, several of these proteins are processed and presented by the MHC-I, constituting tumor-specific peptides with potential as immunotherapy targets.

The candidate will characterize these neoantigens by testing whether their therapy-induced presentation results in increased cancer cell killing by T-cells in vitro and in vivo. The candidate will also assess the immunogenicity of the neoantigens and study whether these peptides can be exploited for combinatorial treatments of chemotherapy and cancer vaccines. The project will use novel genomic techniques such as ribosome profiling, RNA-Seq, proteomics, and immunopeptidomics to characterize the regulatory role of newly discovered antigens. The results of this project will identify new therapeutic targets with important implications for clinical intervention.