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EPIGENETIC EDITING AS A POTENTIAL THERAPEUTIC TOOL FOR THE TREATMENT OF NONCOMMUNICABLE DISEASES

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Epigenetic editing has a powerful potential to direct reprogramming of cellular phenotype that can be used in disease modeling. The reprogramming of cells from different origin into insulin-producing cells could provide a solution for restoring functional beta cell mass in diabetic patients. We used CRISPR/dCas9-based epigenetic tool for targeted hypermethylation of *Arx* promoter and its subsequent suppression in mouse pancreatic α cell line. By epigenetic silencing of *Arx* we successfully triggered a direct, transient switch of pancreatic α- to insulin-producing cells obtaining approximately 1% of transiently transfected cells which were able to produce 35% more insulin than Mock transfected α cells.
As a future perspective we intend to address the potential use of epigenetic editing tool as a pre-therapeutic approach in triple-negative breast cancers (TNBCs) with unknown mutational signature of *BRCA1*. The *BRCA1* methylation (BRCAness) as a predictor for response to therapeutics such as PARPi would allow direct TNBC treatment without previous screening for *BRCA1* mutations. The main objective will be to induce BRCAness by suppressing *BRCA1* expression in TNBC cells via targeted DNA methylation of *BRCA1* promoter using the synthetic epigenetic editing tool. This approach would enable the faster decision toward the use of newest medicaments to increase cells' apoptosis and cancer cell diminishment.

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