Material and methods: The gold-ion catalyst was linked via an intermediate locking system to an albumin, which was tagged with dozen glycan molecules. It was introduced into 8 to 10-week-old BALB/cAJcl-nu/nu mice via the tail vein ($N = 6$). After 30 minutes, fluorescently labeled propargyl ester probe was injected, abdominal side and dorsal images were taken at 30-minute intervals.

Results: The presence of glycan markers on albumin surface have led to the Au(III) complexes accumulation at targeted organs (liver or intestine) without leaching or deactivation of the metal catalysts. Subsequent fluorescently labeled propargyl ester probe introduction resulted in the target-selective gold-catalyzed amide bond formation between propargyl ester probes and amines on surface proteins. It was proved by the fluorescence ratios of the targeted organs based on the region of interest within a whole body 2 hours after fluorescent probe administration. As a control, mice were also treated with the gold-deficient glycoalbumin complex and propargyl ester, where the probe was immediately distributed over the whole body.

Conclusions: The first example of transition-metal-catalyzed bond formation selectively at targeted organs within a live animal is reported. It was shown that gold complexes can be delivered to target organs in living mice, where they can speed chemical reactions for diagnostic or therapeutic purposes. This method enables various therapeutic molecules to be synthesized directly at the target organs in living organisms.

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P133-F | Development of a panel of pancreatic cancer cell lines expressing doxycycline inducible spCas9

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Background: Pancreatic cancer (PC) is one of the most aggressive types of cancer with high lethality rate due to multiple chemoresistance that has been developing in most cases. Understanding of chemoresistance mechanisms is critical to develop new effective treatment strategies for PC patients. Previously we applied primary drop-out genetic CRISPR/Cas9 screening of pancreatic cancer AsPC-1 cells expressing Cas9 and sgRNA libraries targeting whole-genome and cell-cycle genes to identify genes regulating platinum resistance. We identified 130 genes knock-out of which significantly changed platinum sensitivity (Skripova et al., 2016). In this work we created the panel of PC cell lines expressing doxycycline inducible spCas9 in order to validate 130 nominated genes using newly synthesized focused sgRNA library.

Material and methods: PC cell lines AsPC-1, Panc-1, CFPAC-1, HPAF-II, MIA PaCa-2, BxPC-3 and Capan-2 were transduced by lentivirus containing Lenti-iCas9-neo plasmid encoding a doxycycline inducible of FLAG-tagged spCas9. 0.5 mg/mL of G418 was used to select transduced cells. Western blot analysis with anti-FLAG-epitope primary antibody was used to detect Cas9 expression.

Results: Transduced cells were selected with G418 and single cell clones of each line were obtained. 7–12 clones per each cell line were checked for Cas9 expression after 6 days incubation with 1 μg/mL of doxycycline. 30–95% of clones showed Cas9 expression. Clones with the highest Cas9 expression level were chosen for further work.

Conclusion: Panel of PC cell lines expressing spCas9 including AsPC-1, Panc-1, CFPAC-1, HPAF-II, MIA PaCa-2, BxPC-3 and Capan-2 was created. Created panel is useful for further CRISPR/Cas9 based researches. The panel will be used for validation of 130 genes identified in our previous work as well as for deeper investigation of contribution of individual validated genes in platinum resistance mechanisms.

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P134-F | The effect of small molecule compounds Physcion and PFI-3 on the sensitivity of the tumor cell lines SCC61 and AcPC-1 to cisplatin

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Background: One of the main problems of modern oncology is the resistance of tumors to chemotherapeutic drugs, including cisplatin. One of the most promising approaches to overcome drug resistance is combination therapy. This study was designed to investigate the sensitivity of pancreatic AsPC-1 and head and neck SCC61 cancer cell lines to cisplatin in combination with small-molecule compounds named Physcion [R. Lin, 2015] and PFI-3 [B. Vangamudi, 2015] which are inhibitors of the 6-phosphogluconolactonase (PGD) and bromodomains of SMARCA2/SMARCA4, respectively.