zielten Zylinder einer suspekten Läsion. In der vorliegenden Arbeit wurde die Detektionsrate pro Läsion in Abhängigkeit von der Zahl der entnommenen Proben untersucht.
Material und Methoden: Die klinischen und histologischen Daten aller Patienten die zwischen Oktober 2014 und August 2018 eine robotisch assistierte transperineale MRT/TRUS-Fusionsbiopsie erhielten wurden retrospektiv analysiert. In die Untersuchung eingeschlossen wurden Patienten mit einer Läsion >2 nach PI-RADS. Ein PC ISUP >1 wurde als klinisch signifikantes Prostatakarzinom (csPC) gewertet. Die Detektionsrate für PC sowie csPC in Abhängigkeit von der Zahl der Stanzzylinder wurde untersucht.
Ergebnisse: Bei 582 Patienten wurden 3581 gezielte und 6766 systematisch Biopsien entnommen. Das mediane Alter war 68 Jahre, das mediane PSA 8,0 ng/ml, das mediane Tumorvolumen im MRT 50,0 mm^3. Die mediane PI-RADS Stufe war 4349 (60 %) hatten ein PC, 293 (50,3 %) ein csPC in der kombinierten Biopsie. 237 (40,7 %) hatten ein csPC in der gezielten Biopsie. In der multivariaten Analyse (angepasst für PSA, PI-RADS und Alter) zeigte sich eine signifikante Assoziation von 7–11 gezielten Proben zum Vorhandensein von mindestens 2 positiven gezielten Biopsien (OR: 1,82; $p<0,01$) und mindestens 2 gezielten Zylindern mit csPC (OR 1,63; $p<0,05$). Für über 11 gezielte Proben zeigte sich keine signifikante Assoziation.
Zusammenfassung: Wir konnten zeigen, dass die Entnahme von 7–11 gezielten Zylindern mit einer signifikant erhöhten Detektionsrate verbunden ist. Eine weitere Steigerung zeigte nur eine sehr geringe Erhöhung.

V14 – Prostatakarzinom – Experimentell I

18.09.2019, Kopenhagen 2, 15.00–16.30

V14.1
Inhibition of cholesterol and steroid synthesis via miR-205 target gene SQLE is an intriguing treatment strategy in various progression models of prostate cancer

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Background: Cholesterol biosynthesis is a key feature of prostate cancer (PCa), since it contributes significantly to growth in this entity. Here, we investigated the inhibition of SQLE, a miR-205 target gene and important enzyme for cholesterol synthesis, in PCa.
Methods: Multiplex CRISPR/Cas9 genome editing was applied to investigate regulation of SQLE by miR-205 in PCa cell lines either relying on androgen receptor (AR) signalling or after AR depletion through e. g. chronic treatment with abiraterone. Primary PCa ($n=74$) and lymph node metastasis ($n=22$) tissues were used for validation of inverse expression of SQLE and miR-205. Mass spectrometry with U-^{13}C isotope labelling was used to determine cholesterol biosynthesis. AR transactivation assays and PSA measurements were used to evaluate AR signalling.
Results: We were able to confirm SQLE as an essential target gene of miR-205 and showed that inhibition of SQLE via competitive inhibition or miR-205 overexpression lowered cholesterol biosynthesis and androgen signalling in PCa cells. In tissues, SQLE and miR-205 expression correlated inversely and characterized advanced disease. Inducible knockdown of SQLE showed a significant proliferation inhibition in PCa cell lines whereas stable overexpression exposed significant proliferation/migration advantages, which was accompanied by increased cholesterol biosynthesis and AR signalling. Regarding abiraterone resistant PCa models, competitive SQLE inhibition was still able to inhibit growth and survival, depicting the importance of cholesterol metabolism in every stage of PCa development.
Conclusions: Targeting SQLE is an intriguing novel treatment strategy for PCa. Further experimental work will evaluate the impact of SQLE inhibition in orthotopic in vivo PCa models.

V14.2
miR-221-5p decreases proliferation and migration in human prostate cancer cells and reduces tumor burden in vivo

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Objective: Despite latest advances in cancer therapy, prostate cancer (PCa) remains the third leading cause of cancer-related death in men. Therefore, understanding the processes regulating proliferation, survival and motility of PCa cells is crucial for the identification of new therapeutic targets. microRNAs regulate many biological processes. miR-221 downregulation was associated with PCa progression. Here we studied the effect of miR-221-5p overexpression in PCa cell lines and investigated the impact of miR-221-5p on tumor growth *in vivo*.
Material and methods: miR-221-5p expression was studied in a dataset of PCa patients (GSE21036). miR-221-5p overexpressing PC-3M-Pro4 and C4-2 cells were characterised *in vitro* by proliferation, clonogenicity and migration assays. Expression of selected EMT markers was assessed by western blot. The extravasation potential of PC-3M-Pro4 cells overexpressing miR-221-5p was determined in a zebrafish model. The effect of miR-221-5p overexpression on PC-3M-Pro4 cell growth was studied in an orthotopic mouse model.
Results: miR-221-5p downregulation correlated to PCa and progression in patient dataset. miR-221-5p overexpression reduced proliferation, clonogenicity and migration of PCa cells. Modulation of EMT markers partially explained decreased migration. Diminished levels of miR-221-5p rescued the aggressive phenotype of PC-3M-Pro4 cells, implying that the observed effects were specific to miR-221-5p. Overexpression of miR-221-5p in PC-3M-Pro4 cells reduced tumor burden in zebrafish and decelerated tumor growth in mice.
Conclusion: Our data suggest that miR-221-5p represents an interesting molecule to interfere with PCa growth and progression to incurable, metastatic disease.

V14.3
Downregulation of miR-221-3p mediates overexpression of VEGFR2 in high risk prostate cancer–thereby modulating the response towards therapeutic Tyrosine Kinase Inhibition (TKI) in vitro

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Background: High levels of miR-221 have been associated with resistance towards Tyrosine Kinase inhibitors (TKIs) in renal cell carcinoma and