of 0.54 ($p < 0.001$) between predicted and measured treatment response, while extracted DCEMRI parameters together with volumes and PSA gave a correlation coefficient of 0.66 ($p < 0.001$). The approach where all parameters (DWMRI, DCEMRI, volumes, PSA) were combined was superior to all other BPNN simulations and successfully predicted ultimate treatment response with a correlation coefficient of 0.85 ($p < 0.001$).

Conclusions: The results indicate that the combination of several functional MRI parameters obtained early in the course of treatment, into an ANN model, may provide additional information about therapy response. If established, this approach may help identifying non-responding patients early during treatment course, allowing these patients to be considered for alternative treatment strategies, and, thus, providing a contribution to the development of individualized cancer therapy.

150 Molecular characterization of apocrine carcinoma of the breast: validation of an apocrine protein signature in a well-defined cohort

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Background: Invasive apocrine carcinomas (IACs), as defined by morphological features, correspond to 0.3−4% of all invasive ductal carcinomas (IDC), and despite the fact that IDC are histologically distinct from other breast lesions there are currently no molecular criteria available for their diagnosis and no unequivocal information as to their prognosis. In an effort to address these concerns we have used proteome technologies and IHC to discover specific biomarkers that could allow the characterization of these lesions as well as to dissect some of the steps in the processes underlying apocrine metaplasia and development of precancerous apocrine lesions.

Material and Methods: A panel of antibodies against components of an apocrine protein signature that includes probes against the apocrine-specific proteins 15-PGDH, ACSM1, in addition to a set of markers that are consistently expressed (AR, CD24) or not expressed (ERa, PgR, Bcl-2, and GATA-3) by apocrine metaplasia in benign lesions and apocrine sweat glands (Celis et al. 2008, MCP, Celis et al. 2007; Mol Oncol) was used to analyze a defined cohort consisting of 14 apocrine ductal carcinoma in situ (ADCIS), and 33 IACs diagnosed at the Cancer Institute Hospital, Tokyo between 1997 and 2001. Samples were originally classified on the basis of cellular morphology with all cases having more than 90% of the tumour cells exhibiting cytological features typical of apocrine cells.

Results: Using the expression of 15-PGDH and/or ACSM1 as the main criterion, but taking into account the expression of other markers, we were able to identify unambiguously 13 out of 14 ADCIS (92.9%) and 20 out of 33 (60.6%) IAC samples, respectively, as being of apocrine origin. Our results demonstrate that IACs correspond to a distinct, even if heterogeneous, molecular subgroup of breast carcinomas that can be readily identified in an unbiased way using a combination of markers that recapitulate the phenotype of apocrine sweat glands (15-PGDH$^+$, ACSM1$^+$, AR$^+$, CD24$^+$, ERa$^-$, PgR$^-$, Bcl-2$^-$, and GATA-3$^-$).

Conclusions: The results pave the way for addressing issues such as prognosis of IACs, patient stratification for targeted therapeutics, as well as research strategies for identifying novel therapeutic targets.

151 EpCAM expression on disseminated tumour cells in cancers of the digestive tract

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Background: Being involved in nuclear signaling and due its association with the WNT-pathway, EpCAM is an established immunotherapeutic target for adjuvant therapies with several therapeutic antibodies available. This surface molecule is also frequently used to identify and to isolate cancer cells with stem cell properties as well as circulating and disseminated tumour cells (DTC).

Material and Methods: To investigate whether EpCAM is a potential molecular target for systemic adjuvant therapies in cancers of the digestive tract, we systematically investigated the prevalence of EpCAM expression directly on the target cell population − the DTC. We established a double-labeling technique to visualize CK18 and EpCAM simultaneously on single DTC. Our double immuno-labeling was applied to over 200 bone marrow aspirates from patients with cancers of the digestive tract (including head & neck, oesophageal, gastric, pancreatic, and colorectal carcinoma.

Results: While CK-positive cells were detected in the expected range of approximately 30% of the patients, EpCAM was infrequently expressed on CK-positive cells and was almost never detected in cells without CK-positivity. Compared to the remaining GIT malignancies investigated, DTC prevalence was significantly higher in colorectal carcinoma.

Conclusions: EpCAM expression is infrequent on CK-positive DTC and significantly lower as anticipated from previously published data on EpCAM expression in primary tumours of the investigated entities. Our unexpected findings should be considered in clinical trials investigating the efficiency of systemic adjuvant therapies directed against EpCAM.

152 MDM2 SNP 309 polymorphism is associated with increased risk of initiation and early age of onset in nasopharyngeal carcinoma development

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Background: Mdm2 is the principal negative regulator of p53 targetting its export from nuclei to be destroyed by the ubiquitin-proteasome pathway. Recent studies refer that a recent polymorphism in the promoter region of *MDM2* (SNP309 T/G) has been associated with higher levels of its protein, thus it favors p53-pathway abolishment, cell cycle escape and development of cancer. We aimed to study the role of MDM2 SNP309 T/G polymorphism in the development of Nasopharyngeal Carcinoma development.

Methods: A cross-sectional case control study was developed with 111 patients with Undifferentiated type (WHO type III) Nasopharyngeal Carcinoma (UNPC) and 509 healthy individuals from the North of Portugal. We determined the genetic distribution of the MDM2 SNP309 polymorphism by PCR-RFLP in DNA extracted from peripheral blood samples. Statistical analysis was performed to calculate the Odds Ratio (OR) and 95% Confidence Interval (95% CI) as a measure of association between the polymorphism and the development of UNPC. The genotype-specific distributions according to age of disease onset were tested by calculating the cumulative hazard function plots computed by the Kaplan–Meier methodology with Log-rank and Breslow test.

Results: This study revealed an increased frequency of MDM2 SNP 309 GG homozygous in patients with the undifferentiated type of nasopharyngeal carcinoma, which revealed increased risk (OR = 2.51; 95% IC 1.45–4.34) particularly in the early clinical stages OR = 3.39; 95% IC 1.83–6.26). Moreover, we found that the median age of onset of UNPC cases in MDMD2 SNP 309 GG homozygous was significantly different from T allele carriers (55.2 years old *vs* 61.9; $p = 0.008$) with more effect in early clinical stages (55.3 *vs* 65.3; $p < 0.001$).

Conclusion: Our study suggests that MDM2 SNP309 can be a surrogate risk marker for the development of NPC mainly in early ages and as a initiation marker for potential cancer development.

153 Urological cancers models derived from patients

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Urologic cancers (kidney, bladder, prostate) represent 20% of all cancers (1 300 000 cases) and 15% of cancer-related deaths (500 000 deaths) per year worlwide, with an incidence increasing steadily up to 10%/year. These cancers remain therapy-resistant despite the development of targeted therapies. The emergence of new therapeutic approaches are thus urgently needed. These cancers show high cytogenetic variabilities and are heterogeneous for a same tumour. Because they do not reflect such variabilities and heterogeneity, current models, i.e cell-derived xenografts in immunodeficient rodents or genetically manipulated mice, are inadequate to developp effective therapies. The tumour-derived xenografts in immunodeficient rodents appear today as the missing link between cell-derived xenografts and clinical trials. Indeed, they reflect this heterogeneity and allow to identify predictive biomarkers.

Until now we obtained from the Urology department of the New Hospital of Strasbourg tumour and normal corresponding tissues from 130, 27 and 14 patients with sporadic renal cell carcinoma (RCC), transitional bladder cancer and prostate cancer, respectively. Informed consent and clinical history is available for all patients. Tumour fragments were xenografted in nude mice sub-cutaneously and orthotopically using an improved method kept secret. Tumours that have grown were then grafted sequentially until the eighth passage in nude mice. Xenografts are pursued at a rythm of 50 (RCC) and 25 (bladder and prostate) per year. Tumours were analyzed at the histopathologic and metabolomic levels. The anti-tumour efficiency of sunitinib (obtained from Pfizer), sorafenib and everolimus was analyzed in 8 patient-derived RCC xenografted models tumours.