immunohistochemistry. The optimal imaging regime was then used for a $^{131}$I therapy study.

Chemokine mRNA and protein analysis indicated a substantial increase in expression levels of chemokines and growth factors, involved in MSC tumor homing, after heat exposure. In addition, MSCs showed directed migration towards the supernatant of thermo-stimulated cancer cells. In vivo, with the optimal regime, we observed a significantly increased uptake of $^{125}$I in tumors of heat-treated animals (41 °C) when thermostimulated 24h after CMV-NIS-MSC injection compared to control animals (37 °C). Immunohistochemical staining of tumor sections showed strong tumoral NIS-specific immunoreactivity and RT-PCR an increased NIS mRNA expression in heat-treated tumors, thereby confirming tumor-selective, temperature-dependent MSC migration. CMV-NIS-MSC-mediated $^{131}$I therapy combined with regional hyperthermia resulted in a reduced tumor growth that was associated with prolonged survival of regional heat-treated animals compared to normothermic mice and to the saline control group.

In summary, we have demonstrated a significantly increased, selective MSC migration towards the tumor stroma after regional hyperthermia in the $^{125}$I imaging study. The combination of MSC-mediated NIS gene therapy with mild regional hyperthermia resulting in stimulated therapeutic efficacy of NIS-mediated $^{131}$I therapy.

**Adrenal**

**ADRENAL - TUMORS**

**Adrenal Incidentalomas: Prevalence and Referral Patterns in a UK University Hospital Using Real-Life Data**

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**SAT-174**

The estimated prevalence of adrenal incidentaloma at abdominal CT scan is 0.5-2% (1). However, from clinical practice, we noticed that incidentalomas are referred from other imaging modalities (eg MRI) and of other sites (eg thorax, spine). We therefore explored the relationship between prevalence rates and (i) imaging modality and (ii) its change over time, in a real world clinical setting from a large UK teaching hospital/trauma centre. We also examined the referral pattern of potential lesions to endocrinology. We extracted data from all radiology reports for all CT and MRI scans from Jan 2018-Oct 2019. We utilised a key phrase search strategy (eg adrenal adenoma/lesion/mass/module/incidentaloma, indeterminate adrenal, indeterminate). Where possible we excluded false hits (eg no adrenal lesion). These were linked to the referral patterns as identified by a referral logged or an attendance (new or follow-up) to endocrine clinic 3 months post index scan. Preliminary data showed that, from a total of 127878 scans performed, 2604 potential lesions were reported (prevalence 2.0%), comprising 2496/88838 (2.8%) CT scans and 108/39040 (0.3%) MRI scans. The number of scans/month increased in 2019 vs 2018 (6.9% for CT and 12.6% for MRI). Only 9.0% and 15.7% of reported potential lesions detected by CT and MRI, respectively, were referred for endocrine review. Hence, MRI patients were more likely to be referred than those with CT scans (p=0.018). Referral rates were lower in 2019 than 2018 (8.6% vs 14.4%; p less than 0.001). This approach has its limitations but allows efficiently review of large cohorts. Adrenal incidentalomas pose a rising challenge in view of increasing reliance on scanning. Despite a dedicated adrenal multidisciplinary team with a national track record in improving management of incidentalomas (2), the referral rate of potential lesions is worryingly low and not improving, with >90% of cases overlooked. This work is part of on-going innovation to enhance the pick-up rate for these cases whilst addressing the increased endocrine workload in a cost-effective manner. 1. Barzon L, Sonino N, Fallo F, Palu G, Boscaro M. Prevalence and natural history of adrenal incidentalomas. Eur J Endocrinol. 2003;149:273-285. 2. Hanna FWF, Issa BG, Lea SC, George C, Golash A, Fink M, Ogunmekan S, Maddock E, Sim J, Xyndopoulos G, Fordham R, Fryer AA. Adrenal lesions found incidentally: how to improve clinical and cost-effectiveness. BMJ Open Quality. 2019;In press.

**Genetics and Development (including Gene Regulation)**

**GENETICS AND DEVELOPMENT AND NON-STEROID HORMONE SIGNALING I**

**IIM May Influence Matured Oocytes’ DNA Methylation of PCOS Patients**

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**SUN-715**

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of childbearing age and is the main cause of anovulatory infertility. To increase the number of oocytes obtained, controlled ovarian stimulation (COS) has become a routine choice for in vitro fertilization-embryo transfer (IVF-ET), which is one of the common assisted reproductive technologies for PCOS patients. However, for these patients, there is a high risk of ovarian hyperstimulation syndrome (OHSS). Obtaining in vitro maturation (IVM) of immature oocytes, and then in vitro fertilization and embryo transfer of mature oocytes provides a possible way for people to solve the above problems. Since the IVM technology will expose oocytes to in vitro conditions for a longer period of time, theoretically increasing the risk of the oocytes being affected by the culture environment, further research and explorations are needed for study in gene programming, epigenetics, etc. Therefore, to explore the impact of IVM operation on embryonic development is of great significance for further clarifying assisted reproductive safety and improving IVM operation conditions. Here we focused on DNA methylation reprogramming process which was essential for embryonic development. We tested the DNA methylation of sperm, IVM oocytes and IVM generated early stage embryos including pronucleus,
4-cell, 8-cell, morula, inner cell mass, trophoectoderm (TE) as well as six-week embryos by Nimble Gen Human DNA Methylation 3x729K CpG Island Plus RefSeq Promoter Array and compared the data with our published genome-wide DNA methylationomes of human gametes and early embryos generated from in vivo maturation oocytes. We showed that IVM embryos show abnormal DNA methylation reprogramming pattern. By analyzing the abnormally reprogrammed promoters, we further found that IVM may affect the functions of demethylation related genes. Oocytes from IVM manipulation were tested with higher DNA methylation levels, and their abnormal methylated promoters mainly enriched in immune and metabolism pathways. Furthermore, we investigated the DNA methylation of TE, which was directly related with implantation process and revealed the abnormal methylated promoters were related with metabolism pathway too. Our data support that IVM may influence the DNA methylene of oocytes, which in turn affects the methylene of their embryos. However, due to the limited number of samples and the inability of the chip to cover all CpG sites, the results of this study require further research and validation.

Thyroid

THYROID DISORDERS CASE REPORTS I

Unplanned Pregnancy Post Thyroid RAI Ablation

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SUN-516

A patient’s pregnancy and fetus are at an increased risk for complications secondary to history of recent RAI ablation and maternal secondary hypothyroidism.

A 31 year old female with a recent history of miscarriage presented with abnormal thyroid function tests and was history of low dose levothyroxine use. She complained of a 3 month history of extreme fatigue, palpitations and 18 pound weight loss at the time of presentation. Her thyroid stimulating immunoglobulin was 9.21 IU/L (0-0.55), free thyroxine 6.2ng/dL (0.9-1.8), free triiodothyronine 20.04 pg/mL (1.8-4.6) with a suppressed TSH 0.01 uIU/ml (0.27 - 4.2). She was started on methimazole. Her 24 hour radioactive iodine uptake was 60% and she subsequently underwent radioactive iodine-131 ablation in capsule form. She failed the ablation after 7 months and remained on methimazole during that duration. Her second radioactive iodine uptake was 58% and she underwent a second RAI ablation. Her TSH was 50 uIU/ml and her free thyroxine was 0.1 ng/dl. She was started on levothyroxine for replacement. Patient unexpectedly became pregnant approximately six weeks after her radioactive iodine treatment.

Studies have shown that with the exception of miscarriages, there is no evidence that exposure to radiiodine affects the outcome of subsequent pregnancies and offspring. Although the number of children born of mothers exposed to radiiodine is relatively small, the present data indicates that there is no reason for patients exposed to radiiodine to avoid pregnancy. The only adverse effect observed in the study series is an increased incidence of miscarriages in women exposed to therapeutic radiiodine during the year which preceded conception. The fetus would be at risk due to maternal hypothyroidism.

Discussion: Radioactive iodine exposure does not appear to be associated with an increased risk of miscarriage or abnormal subsequent pregnancies.

Conclusion: Pregnancies achieved after exposure to radioactive iodine therapy do not appear to be at increased risk for negative outcomes. Nevertheless, it is recommended that pregnancy be avoided for 1 year following radioactive iodine therapy to allow reproductive function to normalize.

Tumor Biology

TUMOR BIOLOGY: GENERAL, TUMORIGENESIS, PROGRESSION, AND METASTASIS

The Intermediate Prolactin Receptor Is a Breast Cancer Oncogene

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SAT-130

Epidemiological, cellular, and genetic analyses indicate the hormone prolactin (PRL) and its cognate receptor in humans (hPRLr) are significantly involved in breast cancer pathogenesis. Recent evidence demonstrated that a truncated mouse PRLr (mPRLrT) is oncogenic when expressed with canonical long mPRLr (mPRLrL). mPRLrT shares significant sequence homology with a naturally-occurring and widely-expressed hPRLr isoform, the intermediate hPRLr (hPRLrI). As determined by tissue microarray (TMA), hPRLrI is expressed in >85% of breast cancer, with expression increasing as a function of both tumor grade and Ki67 status. To confirm the oncogenic potential of hPRLrI, isoform-specific hPRLrI knock-down (KD) was performed in breast cancer cell line MCF7. hPRLrI KD resulted in a significant decrease in proliferation, migration, and anchorage-independent growth. Given the homology between mPRLrT and hPRLrI, we hypothesized hPRLrI may similarly induce transformation, when expressed alongside wild-type long hPRLr (hPRLrL). hPRLrL/I co-expression in the immortalized but not transformed human breast cell line MCF10A resulted in a significant increase in proliferation, migration, and anchorage-independent growth. These results were not observed following overexpression of either isoform alone, demonstrating that hPRLrL/I co-expression is necessary to induce transformation of normal mammary epithelia. To test our hypothesis in vivo, we established MCF10A xenografts using female NSG mice. Following intraductal injection, we observed rapid tumor growth in the hPRLrL/I cohort, significantly over that of expressing either isoform alone. To determine mechanisms of transformation, we examined both differential protein stability and altered signaling events. In analyzing receptor degradation, a cycloheximide assay revealed hPRLrL stability is increased when heterodimerized with hPRLrI. hPRLrL turnover is impaired in breast cancer, indicating this phenomenon may be involved in the observed hPRLrI-mediated transformation. Regarding differential signaling, we examined the Jak2/Stat5a pathway. Jak2 is a promiscuous