**043**

Mechanism of action of propranolol in Infantile Hemangioma: New insights from a xenograft model

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8 years after propranolol was found efficacious in infantile hemangioma (IH), therapeutic mechanisms remain elusive. It has been shown, in an ovarian cancer model, that ADRB2 signaling is key for chronic stress induced tumor growth. In this model, tumor promotion is abolished by propranolol or ADRB2 siRNA but not by ADRB1 siRNA. In IH patients, after oral administration of 3 mg/kg/day of propranolol, plasma Cmax is below 1 µg/L whereas propranolol has been used in vitro at 100 µM and up to 50 mg/kg in mouse models. Thus, an animal model which recapitulates propranolol response at clinical doses is still needed. We have chosen to develop an in vivo human xenograft model of malignant neonatal tumor (glioblastoma) which is very angiogenic and selectively ADRB2 positive. In such a model tumor hypoxia can be induced by the anti-VEGF-A hevacumab (Avastin). In our model, 2 mg/kg/day of propranolol, or ADRB2 knockdown, induces a modest inhibition of tumor induction but has no effect on ongoing tumor. The gene-expression of the tumor is only changed. Unchanged propranolol doses ranging from 2 to 50 mg/kg we observed an inverse dose response which has been already shown for peristaltic pressure. Elevated HIF1α in IH suggested strongly that a hypoxic environment can explain the specific response of IH to propranolol. Indeed, in the context of relative hypoxia induced by Avastin, our tumor model responds with markers shared by IH such as HIF1α, GLUT1 or MMP9. In that situation, ADRB2 knockdown as well as low dose propranolol gave a significant improvement of tumor growth. Furthermore, we could show that both propranolol and ADRB2 knockdown mediate an attenuation of MMP9 expression. Interestingly, CREB1, which is a cAMP dependent transcription factor known for binding MMP9 promoter, was also downregulated both by propranolol and ADRB2 knockdown. Moreover potential gene-mediated propranolol-antitumoral response also involved in the specific therapeutic response first evidenced in IH.

**045**

Pсориаз и добавления: a neglected challenge

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Pсориаз affects up to 4% of the general population with an enormous socio-economical impact. Within the last few years substantial achievements have been made in understanding the pathogenesis of pсориаз, which led to the approval of a number of highly effective drugs. However, only a proportion of pсориаз patients actually receive best medical treatment. To investigate the association of pсориаз and its possible negative impact on treatment compliance, we screened pсориаз patients for the most common addictions in the general population. The results were then compared to the federal report on prevalence of addictions in Germany 2015. Of 102,796 patients, 57 showed addictive behaviour measured with the used screening tools. Thereof, 41% were regular smokers, 24% high risk drinkers, 11% at risk for drug abuse, 4% at risk for food dependency and 19% compulsive gamblers. Compared to the general population addictions were significantly higher for alcohol abuse (p<0.005), nicotine (p<0.00005) and gambling (p<0.0001). In addition the body mass index was increased in the study population (p<0.0001). Screening measures for addictions have to be promoted for the assessment of pсориаз and can be recommended for all doctors treating patients with pсориаз. Addictions negatively affect treatment compliance and might contribute to the undertreatment of patients with pсориаз in general. Parallel to new drug approvals and even more detailed insights into pathomechanisms of pсориаз, public health strategies and interdisciplinarity approaches are essential for the future of sustained pсориаз healthcare.

**047**

Validation of the Self-Assessment Vitiligo Extent Score (SA-VES) as a patient reported outcome

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The Vitiligo Extent Score (VES) has been introduced recently for the clinical assessment of vitiligo extent. We developed a simplified version of this structured instrument as a self-administered tool (SA-VES) for patients. Patients were asked to fill in the scoring template and were invited to complete this again after 2 weeks. In addition, clinical pictures of vitiligo patients were taken at dermatologists using the SA-VES. Ninety-two patients completed the form twice. The SA-VES demonstrated a very good intra-rater reliability (intraclass correlation for BSA = 0.868 (95% CI: 0.693-0.947). According to the patients this evaluation method was easy and fast (71% the 10-item version as the best option) (97%) and 10-item version (87%) of the SA-VES demonstrated a very good inter-rater reliability for 91% of the patients (95% CI: 0.788-0.963). The results of this study support the general validity of the SA-VES and demonstrate that the SA-VES has excellent correlation with its investigator-reported counterpart (VES). This patient oriented evaluation method may be useful in daily practice and epidemiological studies.