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Abstracts

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Annotations
In the following we are publishing the abstracts as submitted by the authors. Missing session numbers represent sessions with no abstracts associated. Missing presentation numbers represent withdrawn or embargoed papers or abstracts, which have not been received or requested as per date of printing.

Keys and abbreviations

S.01.01 Oral Presentation

P.01.01 Poster Presentation

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role of Wnt signaling and identify molecular mechanisms operating during OS development.

Methods: An inducible bone-specific Wntless (Wls) loss-of-function OS model was generated by combining *wls* floxed, Osx-Cre with the *H2k-c-fos-L*TR (*Fos*^{Tg}) genetically-engineered mouse model for OS (Wls^{deltaOB}-OS mice). Tumors were monitored longitudinally by micro-CT. Gene and protein expression were visualized by quantitative RT-PCR and immunohistochemistry, respectively. Collagen fibers was performed by sirius red staining and polarized-light microscopy.

Results: In bone tumors from *Fos*^{Tg} mice, the canonical Wnt target gene, *axin2* was decreased, while the non-canonical Wnt ligands *wnt7b* and *wnt9a* were increased. Importantly, tumor burden was decreased in Wls^{deltaOB}-OS mice compared to *Fos*^{Tg} mice, with an obvious effect on tumor number. Furthermore, Wls^{deltaOB}-OSs grew slower than *Fos*^{Tg} OSs *in vivo*. While the majority of OS developing in *Fos*^{Tg} mice appeared osteoblastic and expressed Osteocalcin (Ocn) and the Lysyl oxidase-like 2 (Loxl2) collagen cross-linking enzyme, OS from Wls^{deltaOB}-OS mice were enriched in fibroblastic cells surrounded by collagen fibers and expressed less Ocn, Loxl2 and *axin2*.

Conclusions: Increased expression of *wnt7b* and *wnt9a*, which are important for bone and cartilage development, is a feature of *Fos*^{Tg}-OS. Genetic inhibition of Wnt ligand secretion decreased tumor burden and affected OS histology and extracellular matrix deposition, indicating that non-canonical Wnt signalling is important for OS development.

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S05.3

EGFR is required for FOS-dependent bone tumor development via RSK2/CREB signaling

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The Epidermal Growth Factor Receptor (EGFR) is overexpressed or mutated in human carcinomas and glioblastomas, which are tumors of epithelial and glial origin, respectively. Human OS also show high EGFR expression, however its clinical relevance is still unclear. Moreover, we have recently shown that EGFR plays an essential role in bone development and osteoblast function. Here we employed an autochthonous cFos-dependent- OS mouse model (H2-*c-fos*LTR) and human OS tumor biopsies for preclinical studies aiming to identify novel biomarkers and therapeutic benefits of anti-EGFR therapies. We found that both osteoblast-specific deletion and inhibition of EGFR leads to reduced c-Fos dependent tumor formation. At the molecular level, EGFR is essential for tumor cell proliferation and endogenous *c-fos* expression via RSK2/CREB signaling. Importantly, Egfr and c-Fos also play an important role in human OS, as coexpression- of both proteins in tumor sections correlated with significantly reduced survival in patients suffering from primary OS. Preclinical studies using orthotopic human OS xenografts revealed that only tumors expressing both EGFR and c-Fos responded to anti-EGFR therapy. Thus, our data demonstrate that EGFR signaling is essential during c-Fos-dependent OS development and that cFos- can be considered as a novel biomarker predicting response to anti-EGFR treatment in OS patients.

S05.4

Bone mineral density in early post-menopausal women does not predict breast cancer risk and mortality: a long-term follow-up study

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Background: Many studies in foremost elderly post-menopausal women have claimed that bone mineral density (BMD) and breast cancer risk are positively correlated. We herein examined this hypothesis in a population of early post-menopausal women participating in a medical prevention program in western Austria.

Methods: Between May 1991 and February 1999, lumbar spine BMD was measured by dual energy X-ray absorptiometry (DXA, N = 1,163, mean age 56.9 ± 5.7 years) or quantitative computer tomography (QCT, N = 2,283, mean age 56.8 ± 5.4 years) in 3,446 women ≥ 50 years. Data on medication and lifestyle factors were collected by questionnaire. Participants were prospectively followed up for breast cancer incidence. Moreover, breast cancer patients were followed up for mortality. Cox proportional hazards models served to calculate risk of breast cancer and mortality.

Results: During median follow-up of 20.7 years, 185 invasive breast cancer cases and 22 deaths due to breast cancer occurred. Risk of breast cancer in the highest vs. the lowest BMD quartile was non-significantly reduced in particular when follow-up was restricted to 10 years (HR 0.53, 95%-CI 0.25–1.12). There was no risk reduction when follow-up began not until 10 years after BMD measurement. There was no association between BMD and all-cause or breast cancer-specific mortality among breast cancer patients.

Conclusions: Our findings challenge the hypothesis that BMD is reflective of estrogen exposure and predictive of breast cancer risk, at least in young post-menopausal women. Confounders like vitamin D might underlie low breast cancer risk at high BMD, thus mirroring better health status.

S05.5

STAR RF-ablation for the management of painful vertebral bone metastases

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