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INTRODUCTION

Bone metastasis are notoriously hard to treat and tend to survive treatment due to drug resistance caused by the bone microenvironment [1,2]. Here, we focus on breast cancer and non-hodgkin lymphoma (NHL), which are known for metastating to bone.

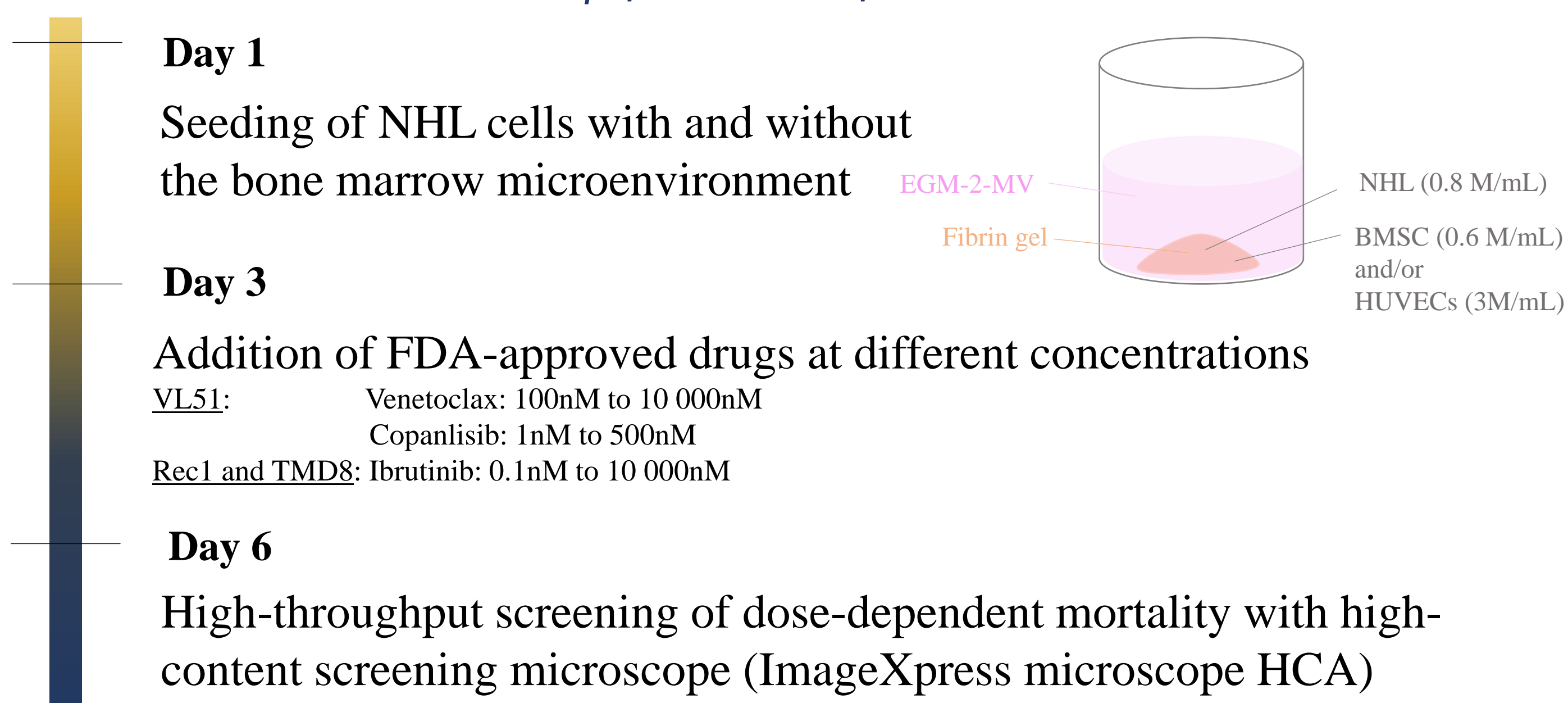
Current drug-testing models are not complex enough to accurately recapitulate the bone biology and architecture.

Based on previous models designed in our lab [3], this project focuses on the biofabrication of 3D human bone model for drug screening with two structures of different stiffness (high-stiffness ion-coated structure for bone cells differentiation and low-stiffness hydrogel for vessel formation)

METHODS

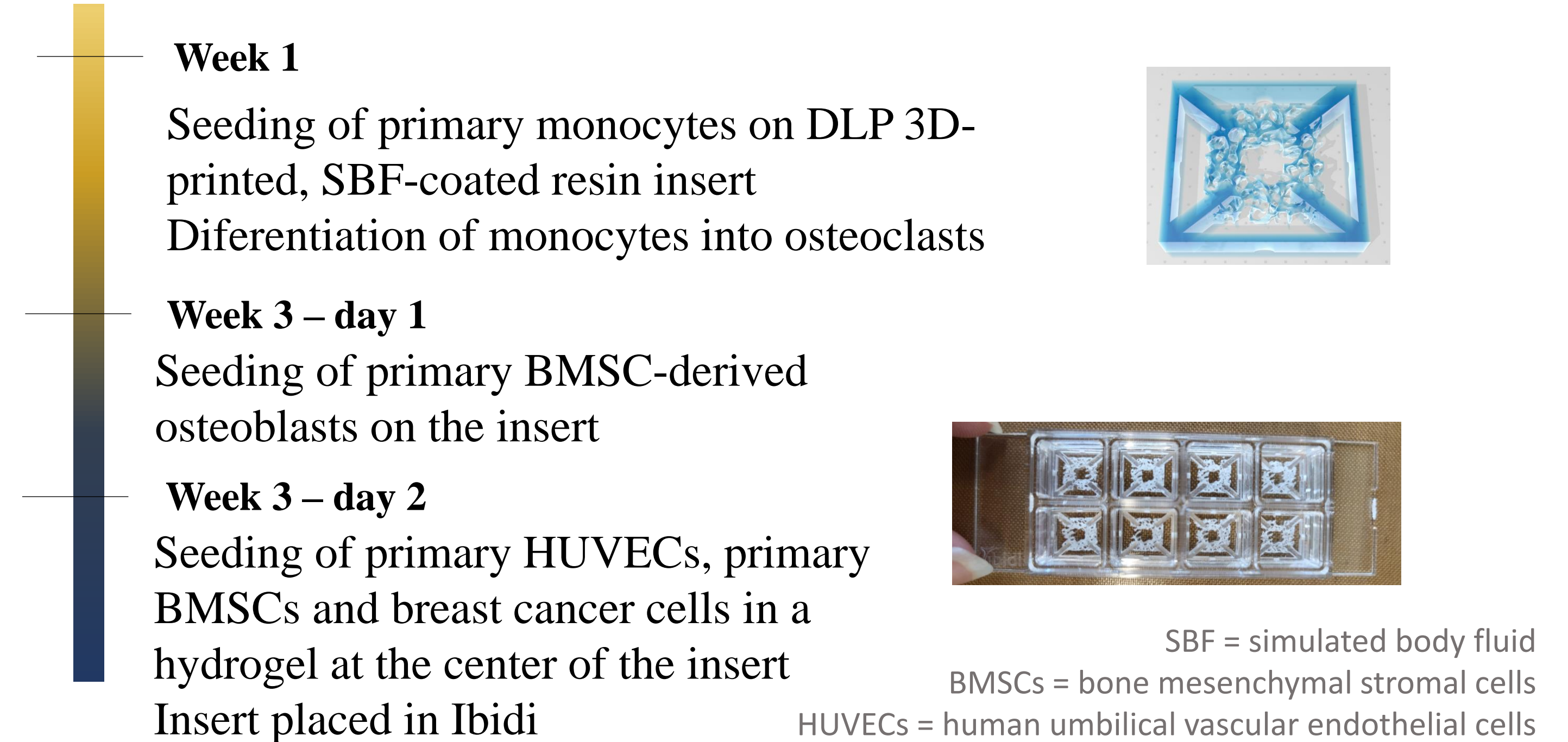
Non-Hodgkin lymphoma

Simplified version of the model



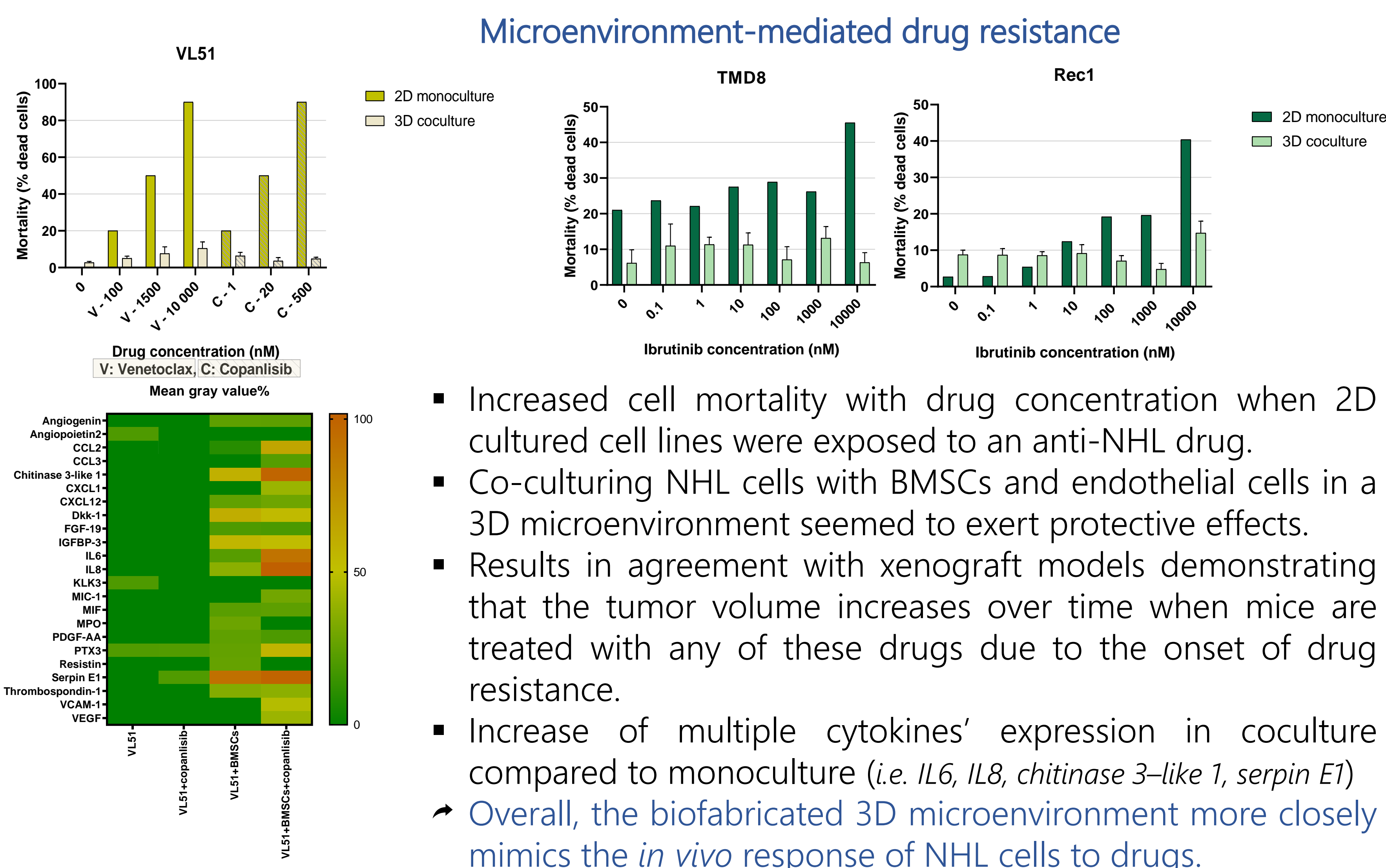
Breast cancer

Addition of osteoclasts and osteoblasts

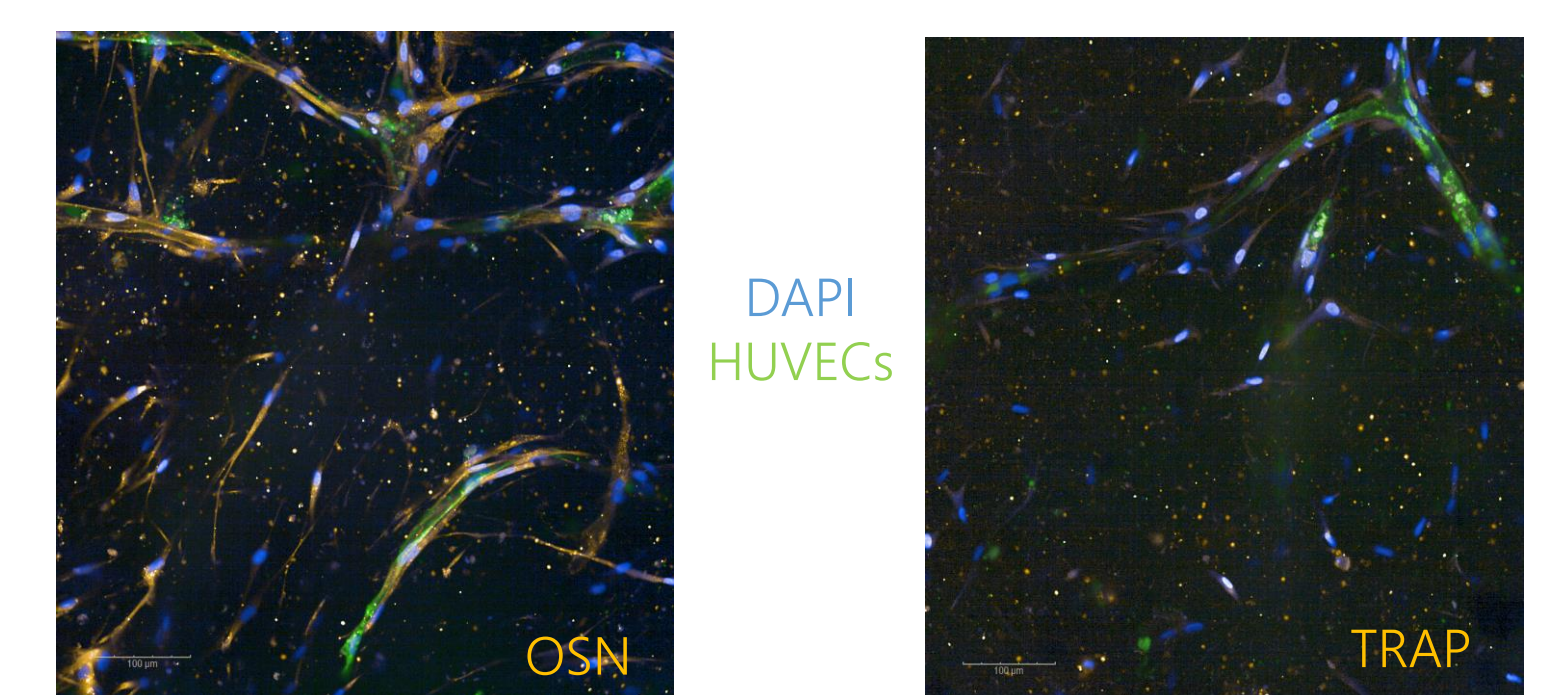


RESULTS

Cancer cell proliferation & drug resistance - NHL

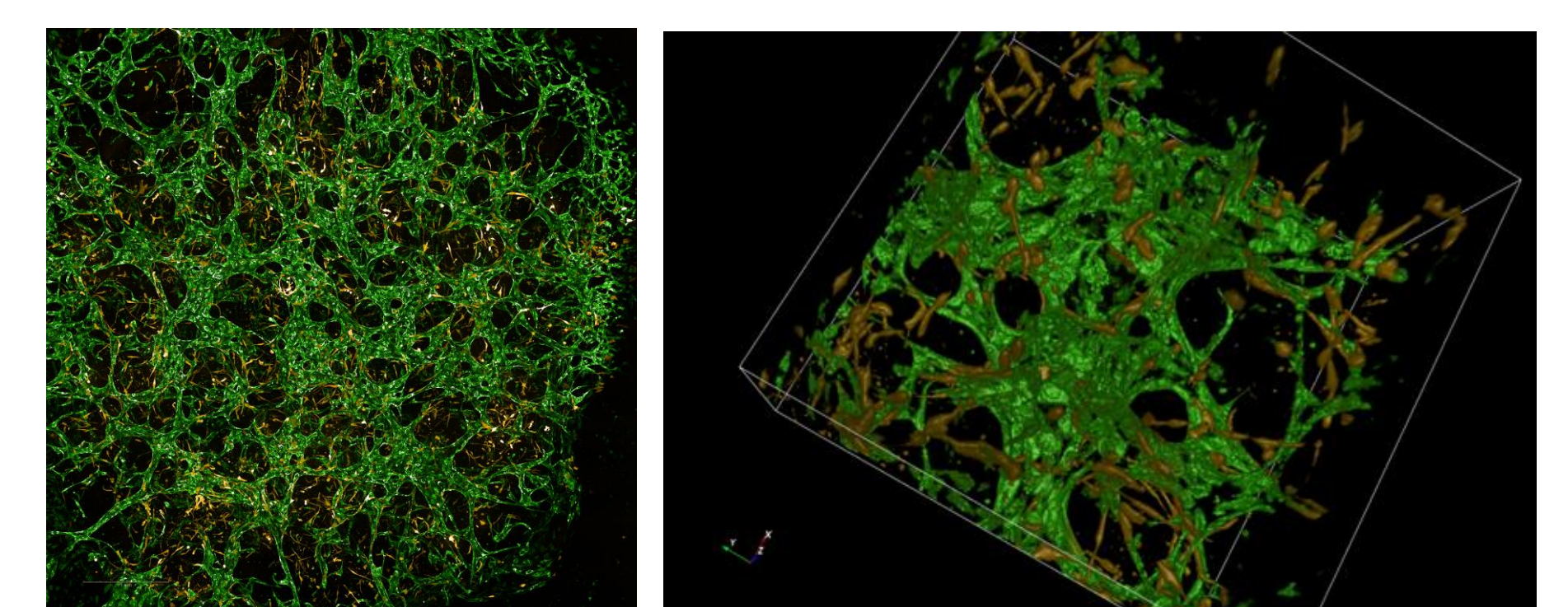


Endosteal niche cell activity



Endosteal niche shows sign of proper tissue maturation and expression of bone activity markers: Osteonectin (OSN) for OBS (left) and TRAP for OCs (right)

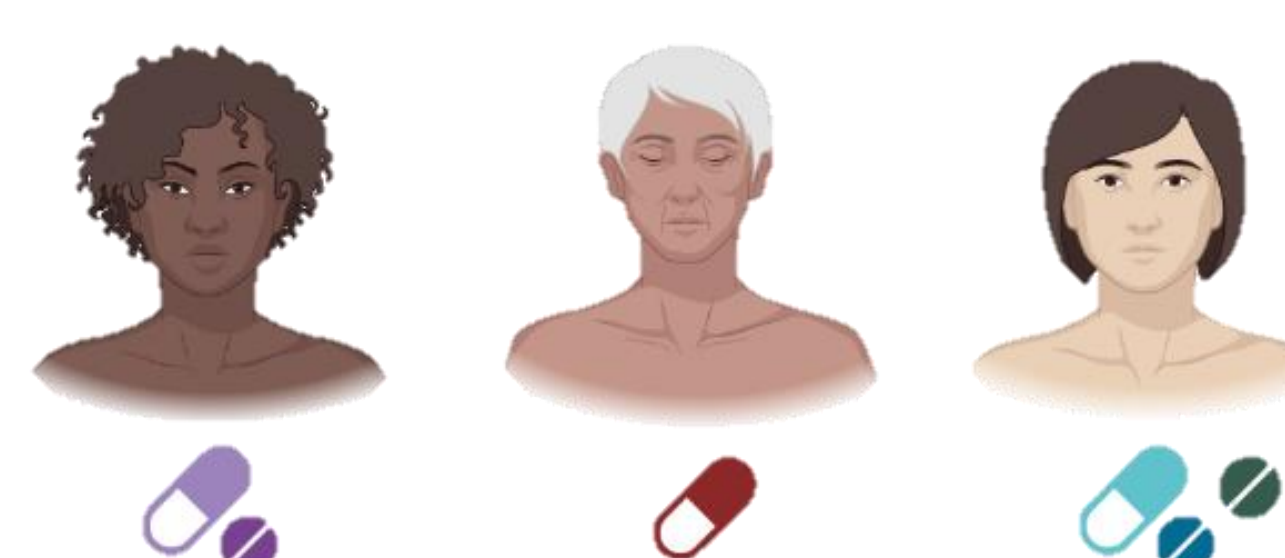
Perivascular niche organization



In co-culture of HUVECs and BMSCs, presence of vascular network throughout the whole gel + presence of lumen in the vessels

CONCLUSIONS

This bone-on-a-chip is able to develop a fully-formed vascular network in less than 4 days and shows the preservation of differentiation markers of bone cells. It also allows for the clustering and proliferation of cancer cells (i.e. breast cancer and NHL cells), as well as highlights the existence of microenvironment-mediated drug resistance.



This model could be used for drug screening or personalized medicine. It would allow to predict which compound, dose and combination would suit each patient best. This would improve the patient's quality of life by enhancing the chance of sensitivity to the drugs as well as reducing side effects.