Results and Discussions
Using this model, the functionality of the different subpopulations of macrophages to affect spheroid growth was proved. The comparison of their volumes at day 7 demonstrates a major difference in growth between the M1 and M2-containing spheroids, the latter having a volume three times larger than that of the M1-containing spheroids. Furthermore, the M1 spheroids presents a higher apoptotic profile than M2 ones. In addition, HNC cells in 3D culture recreates an invasive and immunosuppressive TME and induced polarization of macrophages into M2-like phenotype with high CD206 expression and low CD86 and HLA-DR levels. On the other hand, we showed that bufalin can function as an antitumor immune modulator that governs the polarization of TAMs from tumor-promoting M2 toward tumor-inhibitory M1.
Conclusion
The 3D co-culture constitutes a helpful tool to study tumor-immune cell interaction as well as macrophage plasticity, and to assess the effect of bufalin treatment. Because of its inhibitory impact on tumor cell growth, bufalin treatment could be combined with conventional therapies against cancer cells and could be beneficial in improving patient survival.

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Transcriptional consequences of driver mutations in chronic liver disease

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Introduction
Non-alcoholic fatty liver disease (NAFLD) is the most important risk factor for hepatocellular carcinoma. NAFLD is characterized by excessive hepatic steatosis, is often accompanied by obesity and metabolic syndrome and is estimated to affect one-quarter of the world's population. We previously sequenced 1590 whole genomes from healthy and diseased livers, focusing predominantly on NAFLD. We identified recurrent mutations in genes implicated in insulin signalling and fatty acid metabolism, notably FOXO1, CIDEB and GPAM. We hypothesized that mutations in these genes allow the mutant cells to evade lipotoxicity resulting from chronic caloric excess, thereby providing the cells with survival advantage. In this study we extend the sample cohort and identify new genes under positive selection in NAFLD. Furthermore, we integrate spatial transcriptomics and genomic profiling on adjacent tissue sections to characterize the gene expression profile of mutant clones.
Material and Methods
Liver tissue was collected from multiple Couinaud segments across 3 donors with NAFLD. To annotate driver mutations across tissue sections, 669 microbiopsies were collected using laser-capture microdissection and sent for whole exome or whole genome sequencing. To increase statistical power for identification of genes under positive selection, we combined somatic variants with those from 1560 previously sequenced genomes. To study functional consequences of driver mutations, we performed 10x Visium on adjacent tissue sections and applied differential gene expression analyses on wild-type vs mutant clones.
Results and Discussions
Through whole genome and exome sequencing, we identify seven additional genes under positive selection, three of which (INSR, FASN and A1CF) are implicated in insulin signalling and fatty acid metabolism pathways. Additionally, we identify somatic mutation hotspots in CHD4, a chromatin remodelling enzyme. Finally, we characterize the impact of driver mutations on global gene expression. FOXO1 and CHD4 mutant nodules show similar transcriptional profiles and are frequently mutated across the whole liver within the same patient, suggesting convergence on the same phenotypic properties. We describe transcriptional signatures associated with driver mutations.
Conclusion
Here we demonstrate that clonal expansions promoted in the context of chronic lipid overload can dominate the clonal architecture of the entire organ, without malignant transformation. We show how metabolism is reprogrammed in mutant clones.

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PlexinB1 deficiency in the microenvironment inhibits tumor growth and metastatic dissemination in mouse models of triple negative breast cancer.

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Introduction
Semaphorins and Plexins, originally characterized as axon guidance cues, have been shown to play a critical role also in cancer development. A number of so-called "immune"-semaphorins play a major part in immunological diseases pathogenesis and in shaping the so-called tumor microenvironment (TME), that dynamically regulates cancer progression and impacts on the therapeutic outcome. SEMA4D for instance, was initially described for its role in the immune system, and its targeting in solid tumors has been attempted with controversial outcomes. Nevertheless, so far, the role of SEMA4D high-affinity receptor PlexinB1 (PLXNB1) in the TME has been poorly addressed.
Material and Methods
Our work focused on understanding the role of PLXNB1 in the TME and its contribution to tumor progression, in metastatic triple-negative murine breast carcinoma models.