tiation, while inhibition had the opposite effect, suggesting that Piezo1 has an effect on stem-like phenotype maintenance. Furthermore, we have modified the U251 cell line to have Piezo1-KO and Piezo1-overexpressing cells (via CRISPR-Cas9 and CRISPR-SAM, respectively) and analyzed their viability, colony formation capacity, migration, and cell cycle arrest. Finally, we are developing a Tg.Piezo1/GFAP-cre mouse model to explore the effects of Piezo1 overexpression in glial cells in vivo in terms of neuroinflammation and tumor development.

9. Histone-Deacetylase 8 Drives the Immune Response and the Growth of Glioma

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Many epigenetic modifications occur in glioma, in particular the histone-deacetylase class proteins play a pivotal role in glioma development, driving the proliferation rate and the invasiveness of tumor cells, and modulating the tumor microenvironment. In this study, we evaluated the role of the histone deacetylase HDAC8 in the regulation of the immune response in glioma and tumor growth. We found that the inhibition of HDAC8 by the specific inhibitor PCI-34051 reduces tumor volume in glioma mouse models. We reported that HDAC8 modulates the viability and the migration of human and murine glioma cells. Interestingly, HDAC8 inhibition increases the acetylation of alpha-tubulin, suggesting that this epigenetic modification controls glioma migration. Furthermore, we identify HDAC8 as a key molecule that supports a poorly immunogenic tumor microenvironment, modulating microglial phenotype and regulating the gene transcription of NKG2D ligands that trigger the natural killer cell-mediated cytotoxicity of tumor cells. Altogether, these results identify HDAC8 as a key actor in glioma growth and the tumor microenvironment and pave the way to a better knowledge of the molecular mechanisms of immune escape in glioma.

10. Investigating the Feasibility of Assessing Magnetization Transfer Properties of Distinct White-Matter Connections

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Magnetization transfer ratio (MTR) maps can be associated to the myelin content of the tissue: the higher the MTR, the higher the myelin content. However, in white matter regions where multiple fiber populations, i.e., bundles, can cross the same voxel, the MTR value is voxel- rather than bundle-specific. We propose a method that allows for the assessment of bundle-specific MTR by combining a co-encoded diffusion and MT weighted sequence with Convex Optimization Modeling for Microstructure Informed Tractography (COMMIT), a framework allowing for the estimation of bundle-specific tissue properties. Four healthy subjects (HS) were imaged with a T1w sequence and a novel MT-prepared diffusion-weighted (DW) sequence (MTon). An identical DW sequence, without MT-preparation, was also acquired (MToff). T1 images were segmented in 85 grey matter regions with FreeSurfer and registered to the DW data. A probabilistic tractogram was reconstructed from MToff data and the COMMIT model was then fitted to Mtoff and Mton data separately. Two connectomes, for the Mtoff and Mton data, were calculated by grouping streamlines connecting the same region pair. An MTR weighted connectome was subsequently calculated with element-wise operation on the two connectomes (MTR = (MToff − MTon)/MToff), thus allowing to calculate a bundle specific MTR value. The proposed method was compared to tractometry which, for each streamline in a specific bundle, averages the MTR values along the streamlines path. In all the four HS, in some representative bundles that belong to the left motor network, the MTR values estimated with COMMIT are higher for the bundles connecting the left precentral gyri (L-PrCG) with the medulla (which is a heavily myelinated bundle) than those that connect the L-PrCG with the left subcortical nuclei. In contrast, the tractometry approach appears flat. By applying COMMIT to an innovative dual-encoded MT-dMRI weighted sequence, it is possible to measure bundle-specific MTR.

11. Development of a Frontotemporal Dementia Computer-Aided Diagnostic Tool Using a Dense Convolutional Neural Network on 3D Brain Scans and Explainable Artificial Intelligence Methods

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Despite artificial intelligence (AI) being a leading technology in biomedical research, real-life implementation of AI-based computer-aided diagnosis (CAD) tools into the clinical setting is still facing obstacles. In particular, CAD tools lack standardization practices, leading to poorly reproducible results. This heterogeneity in development is frequently associated with unexplainable results, as deep learning (DL) is often considered a "black box" AI technology. Here, we present the development of an easily reproducible and fully explainable CAD tool using the Clinica and MONAI frameworks and the explainable AI methods (XAI). In particular, a deep learning (DL) convolutional neural network was trained to detect frontotemporal dementia (FTD) on 3D neuroimages from the NIFD database to ensure reproducibility. The DL pipeline includes the preprocessing and the augmenting steps of the 3D images, as well as hold-out cross-validation. The DL convolutional neural network (CNN) achieved a performance comparable to other FTD classification approaches, yielding 0.80 accuracy (95% confidence intervals: 0.64, 0.91), 1 sensitivity, 0.6 specificity, an F1-score of 0.83, and an AUC of 0.86, while maintaining full replicability. XAI methods were applied to understand AI diagnostic behavior and to identify regions of the images where the CNN misbehaves. Specifically, attention maps highlighted that the CNN decision was driven by hallmarking brain areas for FTD, which helped us to understand how to improve FTD detection. AI-based CAD tools should be developed with the goal of standardizing pipelines, as varying pre-processing and training methods, along with the absence of model behavior explanations, negatively impact regulators' attitudes