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EX VIVO HR-MAS NMR, IN VIVO MRS-MRI AND MULTIVARIATE ANALYSIS TO HIGHLIGHT BIOMARKERS IN GLIOMAS

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Gliomas account for about 40% of total primitive brain tumors, and discrimination between high and low glioma grade remains a vital diagnostic decision, determining the most effective treatment and having an important impact on patient management and outcome. The in vivo MRS is considered a tool able to help the diagnosis based on MRI in the evaluation of several human pathologies, including cancer. *In vivo* MRS provides the spectra of living tissues, directly correlated to their chemical composition, but it can be used when the molecular markers of tissues are well established by means of a detailed biochemical picture. This last can be derived from the spectroscopic analysis of *ex vivo* biopsy samples using High Resolution Magic Angle Spinning (HR-MAS) NMR technique. The *ex vivo* HR-MAS NMR spectra provide more details about metabolites (aminoacids, carbohydrates, osmolites, organic acids, mobile lipids) than *in vivo* MRS and permits to produce a metabolic picture of the tissues. Accurate biochemical assignment of metabolites will improve our interpretation of HR-MAS data and the translation of NMR tumor biomarkers to *in vivo* studies. 1D and 2D HR-MAS NMR experiments were used to determine metabolites of brain tumor (astrocytoma grade II, grade III gliomas, glioblastomas). We developed this project on gliomas with the aim to gain a better insight into the discrimination among different grades and subtypes using *ex vivo* HR-MAS NMR, *in vivo* MRS, MRI, clinical data and statistical analysis. We report experiments performed on 15 specimen already collected from different grade glioma. Different amount of some small metabolites such as alanine, lactate, glutamine, glutamate, myo-inositol and glycine in two different *ex vivo* high grade glioma samples. The *ex vivo* spectra obtained on samples from different locations, line-broadened in order to be compared with the *in vivo* MR spectrum, obtained from the same selected voxel. A number of metabolites have been identified as potential biomarkers of tumor type; now we need to combine all the *in vivo*, *ex vivo*, histological and clinical data to obtain a unique tumor fingerprints. Results gathered from this study should lead to the development of tools that can facilitate the distinction of tumor types and grade that cannot be readily distinguished by histopathology or by routine neuroimaging.

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METABOLOMICS ANALYSIS OF TARGETED MULTI-COMPARTMENTAL SAMPLES FOR THE DIAGNOSIS OF THYROID CANCER

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The occurrence of thyroid nodules increases significantly since 1990 due to the improvement of the detection techniques (ultrasound-guided fine-needle aspiration technique) [1]. However, the correct diagnosis of thyroid lesions remains challenging since up to 30% of thyroid nodules are classified as "indeterminate" after cytological examination. In this context, a surgical excision is necessary before a definite diagnosis of the thyroid lesions is obtained. Up to about 85% of the patients with indeterminate nodules are finally diagnosed as benign and undergo unnecessary surgery [2]. It is thus important to develop new approaches, which would help in reducing the number of surgical intervention.

Assuming that metabolic variations would pre-empt the development of morphologic modifications associated with malignancy, we have evaluated the potential of NMR-based metabolomics techniques as a complementary tool for thyroid cancer diagnosis.

Our approach focuses on targeted multi-compartmental samples, i.e. tissues excised from thyroid lesions and plasma from peripheral blood, collected from patients with benign and malignant "indeterminate", as well as well-differentiated malignant tumors. Using high-resolution magic angle spinning (HR-MAS) and liquid-state NMR spectroscopy in combination with statistical multivariate analysis (OPLSDA), we obtained distinct biochemical and metabolic profiles from excised tissue and peripheral blood. For both sample types, a clear discrimination between malignant and benign samples was achieved, leading to statistical models with good prediction efficiency [3]. In addition, complementary sets of markers were characterized providing additional information about thyroid cancer metabolic characteristics. Finally, we have explored multidimensional 1H and 13C slow HR-MAS NMR spectroscopy of different types of tissues [4] to improve the preservation of tissue integrity during HR-MAS NMR experiments.

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BIRD'S EYE VIEWING O AND H

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The biological evolutionary development of hos metabolism and physiology as a superorganism. can be significantly affected by alterations in die the microbial symbionts are likely to impact host model system and multi-omics-based approach, colon can prevent death from following enteroher of gut epithelial barrier function [1]. Next, I show pathways of major microbial symbionts affected b microbiome and host metabolism was visualized (DGGE) and NMR profiles from feces [2]. We i collection of a single subject, and integrated the r structure in intravital systems. Our approach prov relevance to personal and public heath care soluti dynamics in the complex microbial community in with environmental metabonomics data.

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THE RELATIONSHIP BETWEEN FITNESS

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Metabolomics is the study of metabolites in biol increasing exponentially. While much effort has profile there is relatively little known about the effe aimed to establish the relationship between fitnes

214 healthy adults aged 18-60 years were recrui sub maximal 4 stages VO_2 test and had detailed were collected. A cohort of 67 subjects (35 mal metabolomics was used to analyse their b luid using an immunoassay. The subject were s in

Statistical analysis of th data revealed gnificant the fitness grou A lysis o e oxyg kinet

Metabol an ysis of the u sam reveale be mo ro unce in the males. A total o the h f nes roup. or males, only 4 amino a bioche an sis of the urine samples which and lepti n the female fitness groups and a sig In conclusion this study demonstrates a relation metabolite changes show that a reduced excretion an increased fat oxidation rate during exercise.