information about physiological mechanism of uptake and transport and allows the quantification of the 99mTc-IDA derivatives excretion by hepatobiliary system. Based on these we studied the HEF as an indicator of human LR of patients with hepatic tumors underwent PH.

Material and Methods: 33 patients (13 W and 20 M; 61,3±11,3 years old) with colorectal metastases (n=25), hepatocellular carcinoma (n=4) and other tumors (n=4) were included. Eight patients (24%) were submitted to a major hepatectomy (MAH) and the others (76%) to a minor hepatectomy (MIH). LR was assessed after intravenous bolus injection of 99mTc-N-(3-bromo-2,4,6-trimethylphenylcarbamoilmethyl 1-iminodiacetic acid (Mebrofenin) that was uptaked by the hepatocytes and eventually excreted via billiary pathway without any change to its chemical structure. The HEF is calculated using deconvolution analysis of first pass curve coming from scintigraphic data. We evaluated the pre-operative HEF (T0) and in the 5th day (T5) and one month after PH (T30). We considered the HEF values of 98.8 ± 0.4% (MED ± SD) as normal. For statistical analysis: t-Student test was used.

Results: 1) The mortality and morbility rates were 0% and 15% respectively; 2) the HEF was 98.33±3.36% at T0, 98.7±2.7% at T5 and 97.9±5% at T30 (no significant differences); 3) the HEF values of the patients submitted to a MAH were 98.2 ± 3.1% at T0, 98.7 ± 2.3% at T5 and 97.1 ± 5% at T30, and for those submitted to a MIH were 98.4 ± 3.1% at T0, 98.9 ± 3.3% at T5 and 98.1 ± 5% at T30 (no significant differences).

Conclusion: These results allows to say that the human LR is early enough to normalize the HEF at day 5 after PH, being this evaluation of undoubtedly interest to know the function kinetics and indirectly knowledge about human LR. Additionally, this fast functional liver recovery has high clinical importance, because more aggressive adjuvant chemotherapy can start much early after surgical treatment.

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Estrogen-associated genes expression in uterine leiomyomas

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Uterine leiomyomas are benign smooth muscle tumors and the most common type of gynecological tumor, representing a significant public health problem. It is generally accepted that these tumors are estrogen dependent because they have the ability to enlarge during pregnancy and to shrink during menopause, ovariectomy, and other hypoestrogeneic conditions. There are only a few studies in the literature regarding hormone regulation and steroid hormone receptor status in uterine leiomyomas. Previous studies suggested that the AHR gene, involved in cell proliferation regulation, is a potential marker involved in uterine leiomyomas. AHR gene codifies the dioxin receptor, which forms dimers with another receptor, the ARNT. The complex AHR-ARNT binds DNA sequences to modulate transcription rates of some genes, including the estrogen receptor. The aims of the present study was investigate the ESR1, ESR2, PGR and AHR mRNA expression in 46 uterine leiomyomas and in normal myometrium using quantitative real time PCR to explore the hormonal molecular basis of these tumors. It was detected a down-expression of all genes: 72% of cases for ESR1, 43% for ESR2, 35% for PGR, and 76% for AHR. In addition, in the 46 cases studied, 63% showed an increased ratio of ESR2/ESR1. The expression pattern was compared to clinical-pathological data, including patient age, age at menarche, number of pregnancies, age at first pregnancy, cycle reproductive phase, race, body mass index features, number of myomas, and localization. It was detected that ESR1 and ESR2 expression levels were statistically associated with race (non-white versus white patients) and that PGR gene expression was higher in patients that presented early menarche. These results suggest that ESR1 and ESR2 may play an important role in the development of leiomyoma and that an imbalance in expression of these receptors may contribute to the pathogenesis of the disease. In addition, AHR gene can be assessed as putative marker in the growth and development of uterine leiomyomas.

Both authors (Reis-Rosa, L.A. and Cirillo, P.R.) have contributed equally.

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Proliferation-associated genes correlated to hormonal receptors and Ki-67 status in breast carcinomas

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The determination of estrogen and progesterone receptors expression status is crucial for the decision on therapeutic strategies. However, the routine evaluation of ESR1 and PGR status by immunohitochemistry shows large interlaboratory variability, particularly when these genes are expressed at low levels. The stratification of breast cancer patients based on characteristic patterns of gene expression associated with ESR1/PGR status is important to improve clinical management and useful to overcome these limitations. Recently, our group reported that breast carcinomas with high Ki-67 expression were significantly associated with tumors exhibiting low levels of mRNA and undetectable protein levels of ESR1 and PGR. In the present study, global gene expression analysis was performed in 68 invasive ductal carcinomas (29 cases: training set; 39 cases: validation set) using the CodeLink Human Whole Genome BioArray (GE HealthCare) platform. The samples were grouped according to ESR1 and PGR expression status measured at both the transcript and protein level as well as to their proliferative index (< 25% and > 25% immunopositivity to discriminate Ki-67- and Ki-67+ tumors, respectively) to explore the implications of the Ki-67 status in defining proliferation gene expression signatures. Using signal-to-noise ratio with permutation and leave-one-out cross-validation, 68 sequences differentially expressed ($p<0.001$) were identified between ESR1-/Ki-67+ and ESR1+/Ki-67- tumor samples. A similar analysis comparing PGR-/Ki-67+ versus PGR+/Ki-67- tumor samples showed 83 sequences differentially expressed ($p<0.001$). A set of 17 genes involved in cell proliferation was identified as differentially expressed in both analyses. A subset of these genes was investigated by quantitative real time PCR (qRT-PCR) in an independent group of samples confirming the oligoarray expression data. Moreover, a significant statistical correlation was observed between gene expression and histologic grade. These data point to a set of genes with a role in increasing the proliferative rate of breast tumor cells, revealing novel potential biomarkers involved in breast carcinogenesis.

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Identification of a gene expression signature correlated to breast cancer prognosis

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Breast carcinoma is a heterogeneous disease with different molecular subtypes being characterized by distinct morphological appearances, genetic alterations, and clinical presentation. This heterogeneity poses a major challenge in its diagnosis and treatment. Breast cancer can also display notorious distinct clinical characteristics in different patient and ethnic populations, having divergent clinical courses despite having similar histopathologic histopathology appearances. Brazilians form one of the most heterogeneous populations in the world, the result of five centuries of interethnic crosses between peoples from three continents: the European colonizers and immigrants; African slaves; and the autochthonous Amerindians. For this reason, molecular signatures of breast carcinomas from Brazilian patients can contribute to identify new molecular markers common at several ethnicities. To this end, global gene expression profiles of a a set of 43 primary breast tumors samples were evaluated using high-density oligoarrays (Platform CodeLink Human Whole Genome BioArray, GE HealthCare). Multiple statistical methods (signal-to-noise ratio with permutation, leave-one-out, t-test) were applied, combining the prognostic information and clinical outcome. Based on clinical criteria and traditional markers used in clinical practice two subgroups of patients were defined: a group of 25 patients were evaluated as “good prognosis”, of which 5 of them presented metastasis; and a group of 18 patients considered of “poor prognosis”, from which 4 of them showed metastasis. The comparison between all patients with metastasis (9 cases) with the group of good and poor prognosis identified an expression signature comprising 52 genes (leave-one-out, $p<0.001$) able to distinguish good prognosis patients without metastasis from patients who had metastasis independent of the molecular prognosis. We also identified an expression signature comprising 134 genes (t-test, $p< 0.02$) able to differentiate patients with poor prognosis that showed no metastasis (for more than five years after the surgical procedure), from patients who developed metastasis. This gene expression signature correctly stratified patients into good prognosis group or poor prognosis group. Differential expression of a subset of these genes was independently confirmed in a larger set of tumor samples using quantitative RT-PCR. Cross-reference of these signature with available breast cancer prognosis signatures such as Oncotype DXtradeTM (Genomic Health Inc.) and MamaPrintTM (Agendia Inc.) showed a limited overlap. These results point to a novel gene expression signature of breast