“BIOMOLECULAR SIGNATURE OF HCC WAITING FOR OLT. IMPACT OF METABOLIC SYNDROME AND CYTOKINE PROFILE.”

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In the context of a PRIER project coordinated by Prof. Giorgio Enrico Gerunda.

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BACKGROUND
Hepatocellular carcinoma (HCC) is the fifth leading cause of cancer death worldwide. Liver transplantation is the only curative treatment in patients with HCC and hepatic cirrhosis. The most critical problem for these patients is the drop-out risk due to disease progression and widening duration in the waiting list due to limited organ availability. Moreover HHC can recur after OLT. Factors underlying HCC progression/more aggressive behaviour and recurrence are still poorly characterized. Metabolic alterations (ie obesity, diabetes) are risk factors for HCC and a recent study has shown that visceral fat accumulation is an independent risk factor for HCC recurrence after OLT. Bio-molecular variability of the tumor might play a key-role in progression HCC and on its recurrence after OLT. Different sets of genes have been associated to different survival rates and metastatic or non metastatic disease and these genes might be modulated by metabolic determinants. No data are available on the relationship between metabolic/cytokine profile, activation of genes controlling glycol-lipidic metabolism, oxidative stress and angiogenesis and HCC progression evaluated through imaging and clinical outcome.

AIM
To evaluate the effect of the metabolic syndrome (MS)/surrogates on the molecular signature and HCC growth/prognosis (survival, recurrence) as related to radiologic features.
Main research field will include:
a) assessment of the role exerted by the presence/history of MS or its components/insulin resistance per se as related to different aetiologies of HCC.
b) impact of MS, steatosis, insulin resistance and cytokines/adipokynes/growth factors profiles
c) relationship with gender and hormonal pattern (estrogens, androgens, adrenal, thyroid, GH, IGF)
d) evaluation of the role specific polymorphisms
**PATIENTS**
All cirrhotic patients (in-patients as well as out-patients) followed up in the Research Units will undergo ultrasonographic (US) screening on a 6-months schedule. Those in whom a lesion compatible with HCC is identified during routine (US) screening, will be enrolled in the prospective imaging and biomolecular study.

**STUDY DESIGN**
The study is a prospective observational cohort study of cirrhotic patients, at first diagnosis of HCC and potential liver transplant candidates. Patient survival and tumor progression will be analyzed in relation with a “molecular signature” defined by analysis of hepatic gene expression (Professor Villa) and related histochemical profile and circulating cytokines.