Conclusions: These results confirm those previously reported in the literature and show the therapeutic potential of rabbit polyclonal antiferritin Ab in relapsed or refractory HL. On the basis of all these results, MATBioPharma proposed to test a radioimmunotherapy with polyclonal antiferritin antibodies (Abs) in patients with refractory or relapsed HL. The treatment is constituted with chelated rabbit polyclonal antiferritin Abs to be loaded with ^{111}Indium for the diagnosis of the tumour(s) by immunoscintigraphy and with ^{90}Yttrium for the treatment of the tumour(s). A phase I study is still ongoing at the Institut Curie/Centre René Huguenin (France) to evaluate the safety and tolerability of ascending doses of ^{90}Yttrium antiferritin until the maximum tolerated dose (MTD) is reached and to select a dose for further investigation (one dose step below MTD). A pharmacokinetics is concomitantly performed to determine dose linearity and pharmacokinetic parameters of increasing ^{90}Y-Ab and Ab. The second dose level will be completed in the third quarter 2007 and available data on immunoscintigraphy, safety, and efficacy of included HL patients will be provided for the 7th International Symposium on HL.

P1

Urokinase-type plasminogen activator receptor variants in serum and plasma of women with various breast lesions

J. Decock[1], W. Hendrickx[1], I. Christensen[2], H. Pappot[3], R. Paridaens[3], G. Høyer-Hansen. *[1]K.U. Leuven, Belgium; [2]Multidisciplinary Breast Centre, University Hospitals Leuven, Belgium; [3]Finsen Laboratory, Denmark*

Background: The urokinase-type plasminogen activator receptor (uPAR) can be detected in blood in both intact and cleaved soluble forms. Several studies reported that an increased level of uPAR in blood is correlated with poor prognosis in various cancers. We examined whether the soluble form of intact uPAR, suPAR (I−III) and the cleaved soluble forms, suPAR (II−III) and suPAR (I), could be detected in blood samples from women with different breast lesions.
Methods: Preoperative serum and plasma was taken from 10 patients in each of the following diagnostic groups: benign breast cancer, carcinoma in situ of the breast, local malignant breast cancer, locally advanced breast cancer and metastatic breast cancer. The protein levels of the various uPAR variants were determined using specific designed time-resolved fluorescence immunoassays (TR-FIA). TR-FIA 1 quantifies non-occupied uPAR(I−III) while TR-FIA 2 measures non-occupied uPAR(I−III) and uPAR (II−III). The levels of uPAR (II−III) can be calculated by substracting the concentrations measured by TR-FIA 1 from those measured by TR-FIA 2. TR-FIA 3 quantifies the liberated uPAR(I).
Results: The levels of soluble uPAR forms in EDTA plasma correlated well with those in serum except for uPAR (I). We found a trend of increased serum and in particular plasma uPAR (I−III), uPAR (II−III) and uPAR (I−III) + uPAR (II−III) levels with the degree of severity of the breast lesion. This observation was most striking for plasma uPAR (I−III) + uPAR (II−III) levels ($p = 0.006$). We have not been able to demonstrate a significant trend for serum or plasma uPAR (I), however this could be a type II error.
Conclusions: The present results indicate that soluble uPAR variants could distinguish breast lesions of different severity and as such could be potentially prognostic markers in breast cancer.

P79

Assessing the utility of matrix-degrading enzymes as a biomarker for disease status and therapeutic efficacy in lung cancer

L. Gandhi[1], A. Exarhopoulos[2], B.E. Johnson, M.A. Moses[4]. *[1]Dana Farber Cancer Institute, Boston, MA, USA; [2]Children's Hospital, Boston, MA, USA; [3]Dana Farber Cancer Institute and Harvard Medical School, Boston, MA, USA; [4]Children's Hospital and Harvard Medical School, Boston, MA, USA*

Background: The matrix-degrading function of several members of the matrix metalloprotease (MMP) family has been implicated as an important step in tumor growth, invasion, and distant metastasis formation. MMPs have been correlated with angiogenesis and tumor progression in several different tumor types. Here, for the first time, we examined the urine of advanced lung cancer patients for the presence of MMP activity to determine whether these markers of invasion could be detected and, if so, whether their levels correlate with disease status and therapeutic efficacy of chemotherapy.
Methods: Subjects with small cell lung cancer (SCLC) or stage IIIB/IV non-small cell lung cancer (NSCLC) were enrolled under an IRB-approved protocol for specimen collection from January-July 2007. Serial urine specimens were obtained prior to initiation of chemotherapy and prior to subsequent cycles until documented progression, study withdrawal, or death. Urine samples normalized for protein content were assessed by gelatin zymography and quantitated by densitometry.
Results: Amongst 10 SCLC subjects analyzed thus far, 8 had detectable MMP-2 activity in the urine and 7 had MMP-9. In addition 5/10 SCLC subjects had larger molecular weight MMP species. Patients with more localized disease (stage IIIB or limited-stage SCLC) had only MMP-2 detectable. Among 12 NSCLC subjects, MMP-2 was readily detectable in 8/13 and MMP-9 was present in 5/13. Initial serial measurements in 5 subjects show 2−5 fold increases in MMP levels during the first months of therapy.
Conclusions: MMP-activity was detectable in a majority of subjects with either SCLC or NSCLC. The limited subset assessed suggests increased levels and numbers of MMP species in widely metastatic disease compared to those with more limited disease. In addition, intra-subject increases in MMP activity were seen in subjects who had initiated chemotherapy, although the relationship of this change to tumor status has yet to be determined. Full longitudinal analyses through the completion of treatment will be presented.
This work was supported in part by an NIH RO1 grant to M. Moses: CA118764−01.

P75

Incidence of familial breast cancer and BRCA mutations in Iranian and Ukrainian breast cancer patients

N.G. Gorovenko[1], C.V. Podolskaya[1], H. Rassi[1], M. Houshmand[2]. *[1]National Medical Academy, Kiev, Ukraine; [2]National Institute for Genetic Engineering and Biotechnology, Theran, Iran*

Background: Breast cancer (BC) is the most commonly diagnosed cancer in Iranian women, and is the leading cancer cause of death in this population but in Ukraine, its incidence rates are 3 times higher than Iran. Both environmental factors and genetics have an impact on the risk of BC. Approximately 90% of breast cancers are sporadic while the remaining 10% are inheritable. Germline mutations in breast cancer-associated gene 1 (BRCA1) have been detected in approximately one-half of the familial breast cancer (FBC) and most of the familial breast/ovarian cancer cases. An accurate evaluation of the penetrance of BRCA1 and BRCA2 mutations is essential to the identification and clinical management of families at high risk of breast cancer. In this article, we consider incidence of FBC and BRCA mutation in Iranian and Ukrainian BC patients.
Methods: Patient samples were drawn from four medical centers in Iran and Ukraine. We retrieved 203 formalin-fixed, paraffin-embedded tissue blocks from women with breast cancer diagnosed, the age of 25−80 years for the years 2004 and 2006. All cases were reviewed using a special questionnaire, which allowed taking into account the presence or absence family history of breast cancer and also other pathology information. Verification of every cancer reported in a relative was sought through pathology reports, hospital records. Multiplex PCR was used to detect the simultaneous detection of three common mutations. For each BRCA mutation, three primers (one common, one specific for the mutant, and one specific for the wild-type allele) were used.
Results: Incidence of familial breast cancer was 32.1% and 28.6% in Iranian and Ukrainian patients respectively. There were no significant differences between cases with regard to incidence of FBC in these populations. The proportion of cases with one of three BRCA mutations (5382insC) was 9% in Iranian breast cancer patients and 9% in Ukrainian breast cancer patients. The hereditary proportions were higher than this for women with at least 1 first-degree relative with breast cancer (19%) in Iranian and Ukrainian patients. There was no statistical difference between Ukrainian and Iranian women with breast cancer diagnosed at age <50 years in term of 5382insC incidence.
Conclusions: Breast cancer risk was strongly related to age, with more than 80% of cases occurring in women over 45 years old. The highest number of cases of familial breast cancer diagnosed was in the 41−50 age group. The relative risk of breast cancer conferred by a first-degree relative with breast cancer was dramaticaly decreased by age. The findings of the present study suggest that 5382insC mutation and family history may have an impact on the incidence of breast cancer in women but because of high relative risk of BC in Ukraine than Iran (nearly 3 times), it is suggest that environmental factors are of greater importance than genetic factors. Our analysis shows testing of 5382insC mutation in breast cancer can be utilized as one of prognosis factors of FBC development risk in these populations.