M.G. Alessio (2), M.B. Donati (1) and T. Barbui (2). Istituto DISSEMINATED
Mario Negri, Milano (1) and Ospedali Riuniti di Bergamo, Bergamo
cysteine proteinase (Falanga Ml to M5 of acute non lymphoid leukemia (ANLL), according to
normal human plasma, the effect being significantly greater
pendent from the presence of FVII and was susceptible to 2
associated procoagulants are considered important in this con­
did not show any procoagulant activity, under the same condi­
cysts proteinase inhibitors (Iodoacetamide, 2 mM, and HgCl ,
from 21 patients with 5 different cytological subtypes (from
coagulants in leukemia.

There is an enhanced incidence (>50%) of severe coagulopathy
in association with several types of acute leukemias. Cell
associated procoagulants are considered important in this con­
text. So far only a Tissue Factor (TF)-type procoagulant has
been described in leukemic cells. We have set up here the ex­
perimental conditions to identify other possible cellular pro­
coagulants in leukemia. We have tested blast cell extracts from 2
patients with 5 different cytological subtypes (from
M1 to M5 of acute non lymphoid leukemia (ANLL), according to
the FAB classification, in order to assay whether they express
"cancer procoagulant" (CP), a F VII-independent FX activating
cysteine proteinase (Falanga & Gordon, 1985; Donati, et al.
1986). All the samples showed the rafication time of
normal human plasma, the effect being significantly greater
(p<0.001) in the M3 group. The activity was 20% to 100% inde­
dependent from the presence of FVII and was susceptible to 2
cysteine proteinase inhibitors (Iodoacetamide, 2 mM, and HgCl ,
0.1 mM) in all of the extracts but the M5 type. In addition, M2
and M3 samples directly activated pure FX in a two stage clotting assay. Control cell extracts from 10 healthy donors
did not show any procoagulant activity, under the same condi­
tions. This study provides evidence for a new procoagulant
expressed by cells of ANLL: the peculiar characteristics of this procoagulant (i.e. its confinement to the malignant pheno­
type, its shedding into the plasma, its possible modulation
by vitamin K antagonist) make this observation of potential
interest in the development of new diagnostic and therapeutic
tools in ANLL.

Tuesday
CANCER AND COAGULATION

DISSEMINATED INTRAVASCULAR COAGULATION (DIC) AND ACUTE LEUKEMIA:
IDENTIFICATION OF A NEW CELLULAR PROCOAGULANT. A. Falanga (1),
M.G. Alessio (2), M.B. Donati (2), T. Barbui (2), T. Casali (2), T. Barbui
(2). Istituto Mario Negri, Milano (1) and Ospedali Riuniti di Bergamo, Bergamo
(2), Italy.

The aim of this study was to investigate the modulation of
procoagulant activity from HL 60 cell line.

Cells were cultured in suspension for 5 days in RPMI 1640 medium
supplemented with 10% fetal calf serum in the absence or in the presence of different concentrations of IFN (100-10.000 u/ml)
at 37°C and 5% CO2 .

Differentiation was assessed by morphological and cytochemical
methods (MGG, ANAE, CAE, MP0) on cytospin preparations and
surface marker analysis with monoclonal antibodies
(GOKM1, M02, M19, M17, M14).

IFN induced morphological and cytochemical changes were
observed at concentrations ranging from 1000 u/ml and higher.

In conclusion, IFN seems to be dependent on
mRNA expression of cellular genes involved in the differentiation of HL 60 cells.


In vitro, heparin inhibits the heparanase activity of HL-60 cells.

In in vivo experiments, we observed that heparin inhibited the formation of lung metastases in mice inoculated with HL-60 cells.

These results indicate that heparin may be a potential therapeutic agent in preventing heparanase mediated extravasation of blood-borne cells.

The present study was undertaken to test the heparanase inhibitory effect of heparin and non-anticoagulant species of heparin that might have a potential therapeutic use in preventing heparanase mediated extravasation of blood-borne cells.

These heparins inhibited less than 5% of the heparanase activity of native heparin. It was found that heparanase abolished its heparanase inhibitory activity while desulfated heparin was able to inhibit heparanase.

When only the N-sulfate groups were desulfated, heparanase activity was restored.

These results indicate that N-sulfate groups of heparin are necessary for its heparanase inhibitory activity but can be substituted by an acetyl group provided that the O-sulfate groups are retained.

Low Mr heparins (main Mr species of 2500 and 4500 daltons) and heparin fragments as small as the tetrasaccharide inhibited heparanase activity.

These results suggest that heparanase inhibitors interfere with tumor metastasis and experimental autoimmune diseases (some heparins are kindly provided by Inst. Chow, Perla and Kabi Vitrum, Stockholm).