infected and tumor cells, and require HLA class I expression on these cells to guide their attack. However, HLA cell surface expression on these cells is frequently switched off, and this has negative effects on immune surveillance. Three major mechanisms may account for undetectable or low HLA class I expression in tumor cells:beta 2m mutation, TPA deficiency, and low factor binding activity specific for the regulatory elements of these genes. Here we describe another molecular mechanism which accounts for the complete absence of HLA class I molecule expression in a tumor line (MSR3-mel) derived from a melanoma patient. Hypermethylation of the MSR3-mel DNA, specifically of HLA-A and -B genes, was identified. This abnormality resulted in loss of HLA class I heavy chain transcription. Treatment of MSR3-mel cells with the demethylating agent 5'-aza-2'-deoxycytidine (DAC) allowed HLA-A and -B transcription, restoring cell surface expression of HLA class I antigens and tumor cell recognition by MAGE-specific CTLs. The MSR3-mel line was obtained from a metastasic lesion of a nonresponding patient undergoing MAGE-3.A1 T cell-based peptide immunotherapy. It is tempting to speculate that the hypermethylation-induced lack of HLA class I expression is the cause of the impaired response to vaccination. The present study showed that DNA hypermethylation could also be a repressor mechanism responsible for the total loss of HLA class I expression in human melanomas, providing a new route of escape from immune recognition.

The results of this study, and the observation that expression of some tumor antigens, is induced by demethylation mechanisms, suggest modulation of DNA methylation as a possible intervention for cancer treatment. However, the high toxicity of the available agents make their use in clinical setting difficult, therefore safe and effective strategies for the therapeutic alteration of DNA methylation are clearly needed.

1507 POSTER

The organisation for the performance of clinical trials at the department of oncology, Uppsala university hospital, Sweden

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Cancer treatment is clearly in need of further development since current therapies provide unsatisfactory results. Clinical trials are a key step in such development and have to be performed efficiently and in correspondence with quality criteria, mainly those of Good Clinical Practice (GCP). This abstract describes the organisation for the performance of clinical trials at our department.

The Research and Development Unit (RDU) at the department of oncology, Uppsala university hospital, Uppsala, Sweden, was started approximately 1 year ago and presently enclose 2 part time physicians (1 oncologist, 1 clinical pharmacologist), 1 part time secretary, 1 full time quality assurance and 7 full time research nurses.

The main purpose of the RDU is to facilitate the clinical research process. Since in Sweden only approximately 10% of all cancer patients participate in prospective clinical trials, an important aim is to stimulate the starting and performance of more clinical trials. Since there is also a need to improve the quality of the clinical trials, notably the "academic trials" (AT), lacking support from the pharmaceutical industry, the RDU has implemented its own Standard Operating Procedures (SOPs) based on GCP, covering all important steps for the planning and performance of cancer trials. One important aspect also covered is the outlining of responsibilities for the investigator and the research nurse within the clinical trial process.

Within the department, the RDU is organised under a Research and Development Council (RDC), with representatives for the department head, physicians in charge of the major tumour groups and the RDU. The RDC assess and approve all clinical trial protocols and their ethical issues and financial agreements prior to start of a new trial. Well started, the RDU should provide full support to the investigator in the performance of the trial. The need for support has naturally been found most pronounced in investigator initiated trials (IIT) and AT.

Through continuous education, both within the RDU and in the department, in GCP theory and practice and critical medical issues related to the performance of clinical trials, the RDU tries to improve its professional and comprehensive support and information to patients participating in clinical trials. The RDU is presently running approximately 40 clinical trials, half of which being IIT or AT, covering the major tumour groups and with emphasis on medical treatment.

1508 POSTER

Allogeneic haematopoietic stem cell transplantation for patients with advanced or refractory multiple myeloma - a chance for cure?

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Introduction: Multiple Myeloma (MM) is a plasma cell malignancy in which high dose chemotherapy followed by autologous stem cell transplantation (SCT) induces a higher response rate and longer overall survival than conventional therapy. Allogeneic transplantation may be curative, but has a limited application because high toxicity and high transplant related mortality. Non-myeloablative regimens are less toxic, allow a rapid and sustained engraftment, maintaining the graft versus myeloma effect that may be enhanced by donor lymphocytes infusion.

Methods: Between November 1998 and December 2000, 7 patients (pts) with MM (6 progressive disease after autologous SCT, 1 refractory disease and low performance status), 5 male, 2 female, median age: 51 years (31-57), underwent a non-myeloablative allogeneic SCT with peripheral blood progenitors from HLA identical sibling. Conditioning regimen was fludarabine (30 mg/m2/dx4), busulfan (4 mg/kg/dx2) and antithymocyte globulin (10 mg/kg/dx4). Cyclosporin was used for GVHD prophylaxis (from day -1 until day +30, then tapered). In order to access the applicability and toxicity of this regimen in our heavily pre-treated pts, we analysed some parameters related with activities of daily living like nourishment, hygienics, communication, occupation and leisure. All pts were transplanted in a room with filtered air, positive pressure and reverse barrier.

Results: All pts engrafted (full/mixed chimerism by STR-PCR) with a median neutrophil count $> 0.5 \times 10^9$/L of 11 days (3-36) and platelet count $> 20 \times 10^9$/kg of 11 days (1-36). Median transfusional support was 4 packed red cells units and 1 platelet transfusion. Median discharge was on day +24 (18-97). Regimen-related toxicity was acceptable with no pts having mucositis grade >3 or hepatic veno-occlusive disease. All pts remained autonomous concerning activities of daily living during admission period. Two pts died (1 from progressive disease 1 year post-allograft and 1 from infection but in complete remission, 6 months after transplant), three pts are in complete remission and two pts are in partial sustained remission. All pts have a Karnofsky performance status $\geq$ 90%.

Conclusion: response rate was high in this group of refractory and heavily pre-treated pts; minimal procedure-related toxicity allowed satisfactory activities of daily living during hospitalisation; the significant improvement in disease status led to a rapid integration in family and social life.

1509 POSTER

Chemotherapy administration: development of a core curriculum

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Purpose: Variations in clinical practice, knowledge levels and skills have been reported by nurses administering cytotoxic drugs (RCN, 1998, Grundy, 1998). For many nurses their knowledge and skills development have been the result of informal experiential learning as part of their job. This situation is unacceptable both professionally and legally and it is crucial that nurses have the appropriate education to undertake cytotoxic drug administration. A core curriculum for cytotoxic drug administration has therefore been developed to address the need for a consistent approach to education in Scotland and provide a framework for future course development.

Methods: The project was commissioned by The National Board for Nursing, Midwifery and Health Visiting for Scotland. Development work was undertaken by a multidisciplinary group with representation from the five cancer centres. The core curriculum has been based on the RCN clinical guidelines for cytotoxic chemotherapy administration. Consideration has been given to nurses' differing levels of involvement with cytotoxic drugs and their different educational needs. The framework has been designed to facilitate the development of courses and content, learning outcomes and clinical competencies have been identified. The core curriculum is currently being circulated as a consultation document.

Conclusion: This paper outlines a national initiative to improve the quality and consistency of practice through education.