The ultimate goal of this project is to develop immunotherapeutic agents that target a patient's own T cells against their cancer. The project took two directions to accomplish this goal: the development of novel single-chain bispecific antibodies and new animal models that more closely resemble human cancers. Although the project has seen some changes in the original plans (such as the focus on a different tumor antigen, the folate receptor), significant progress was made in understanding the effects of this class of immunotherapeutics. In addition, we have developed and now focus on two animal models that provide realistic, albeit challenging, opportunities to evaluate such agents. Our primary findings are that: (1) small, bispecific antibodies with conjugated folate can target folate-receptor-positive tumor cells, both in vitro and in vivo; (2) growth of established transplanted human tumors in TCR/RAG(-/-) mice and endogenous brain tumors in SV40-transgenic mice can be slowed but not cured with bispecific conjugates alone; T cell infiltration into the tumors can be achieved but this infiltration needs to be sustained, and (3) CD28 agonists and CTLA-4 antagonists can be used to sustain T cell activity and an anti-CTLA-4 single-chain antibody was engineered for this purpose.

Heparan sulfate proteoglycans (HSPGs) are a new class of tumor suppressors. The focus of this project is to test novel proteoglycan-based therapies for the treatment of breast cancer. In the first objective, the ability of neoproteoglycans (nPGs) to mimic the anti-tumor activities of naturally occurring proteoglycans is evaluated. Surprisingly, we found that molecules composed of carbodiimide modified GAG chains that differ from nPGs and native proteoglycans in that they are devoid of a protein component inhibit cancer cell viability. These molecules we call neoglycans, inhibit breast cancer cell viability in vitro through the induction of apoptosis. Treatment of established MDA-MB-231 tumors in nude mice with the neoglycan produced from chondroitin sulfate reduced or abolished tumors following a single dose without any apparent toxicity. In the second objective, a gene therapy approach is tested utilizing the HSPG gene syndecan-1. Tagged full length and truncated human syndecan-1 genes have been constructed and subcloned cell lines stably expressing the transgenes have been established and are being evaluated. This project is the first attempt to use HSPG genes therapeutically for anti-cancer therapy. Also as a result of this project, a new class of anti-cancer therapeutics called neoglycans have and continue to be developed.

The text provides information on public health actions funded under 2006 call for proposals in the framework of the programme of community action in the field of public health. The programme is the European Commission's main instrument for implementing the EU's health strategy.
This book is a compilation and discussion of data on the survival of cancer patients in 12 European countries. Measures of incidence, survival and mortality are critical to the interpretation of data on progress in the fight against cancer, and in the evaluation of the overall effectiveness of cancer control programmes. Randomized controlled clinical trials have shown many modern protocols for cancer treatment to be more effective than earlier treatments, but until now, comparable population-based survival figures have rarely been available. EUROCare is a concerted action among European cancer registers, aimed at estimating and comparing the survival of cancer patients in different European populations. The rationale behind this project is to optimize the comparability of survival data by using an agreed and standard definition of the diseases for which survival is to be compared, and by taking due account of basic demographic variables. The EUROCare Working Group succeeded in collecting, checking and editing data on cancer survival from 30 cancer registries in 12 countries, and established a database covering some 800,000 cancer patients in the period 1978-85 and followed up to the end of 1990. This database forms the raw material for this monograph.

Metastatic melanoma and relapsed acute T cell lymphoblastic leukemia remain incurable despite major advancements in our understanding of these cancers. In some ways, the foundation for a cure has already been laid; many molecular targets for drug development are now clearly defined, and recently novel therapeutics have shown promise in the clinical setting. However, this immense progress has not translated into a marked increase in patient survival. This graduate project focused on two aims, which with further research and development may lead to a cure for these cancers. First, the development of a cellular-based high-throughput synergistic assay was looked at, that would allow for rapid screening of multiple drug combinations. Second, cancer-specific alterations in the cell surface high mannose glycoprotein profile were identified in the context of metastatic melanoma and T-ALL cells. The feasibility of these two aims is demonstrated by existing innovations and research. First, protein microarrays have been developed to isolate and characterize a variety of cell types. Second, growth factors and other molecules have been successfully printed onto these arrays. Third, cancer cells and cancer stem cells have been previously shown to have alterations in their cell surface glycome. As part of the first project, micropatterned silane and polyethylene glycol (PEG) coated glass slides were successfully developed, with these modifications acting as a non-fouling surface for cell attachment. On these slides cell-specific antibodies, antiCD3 and anti-GD3, were printed and demonstrated successful capture of T-ALL and melanoma cell lines, respectively. However, the effectiveness of this cell capture needs further improvement, with regards to uniform cell seeding. Future studies will utilize recently developed epoxide coated slides, which allow for covalent attachment of capture antibodies. Additionally, anti-CD4 antibody will be printed for T-ALL cell capture. With respect to the characterization of the cell surface glycome of malignant melanoma and TALL cell lines versus their non- or less-malignant counterparts, we were able to successfully demonstrate that MHC class I and sodium/potassium ATPase proteins were differentially glycosylated on both of these diverging cancers. MHC class I had significantly higher expression on high metastatic potential B 16F 10 cells compared to B16F0 cells (p-value = 0.014), and in Jurkat cells as compared to normal pan T cells (p-value = 0.011). Additionally, sodium/potassium ATPase had significantly higher expression on B16F10 (p-value = 0.028) and Jurkat cells (p-value = 0.013) versus B16F0 and normal T cells, respectively. These proteins, along with other identified high mannose surface proteins are directly linked to cancer cell proliferation promotion. Additionally, the altered glycosylation patterns identified in this graduate project may have a direct impact on MHC class I and sodium/potassium ATPase's roles in cancer cell promotion. Based on obtained data, future studies will focus on confronting the presence of identified proteins on the cell surface through antigen immunofluorescence labeling, and footprinting of high mannose glycans. Footprinting will be done to both determine the extent of glycosylation modifications occurring on cancer cells, as well to characterize any changes in protein conformation due to changes in glycosylation, as determined through in silica modeling.

This project's proof of concept that efficacy and toxicity could be unlinked in immunotherapy began to establish a framework to use for rational combination therapy treatment schedule design, with the goal of treating with each agent when that piece of the immune system is active. Finally, the third project used the Wittrup Lab's system of yeast surface display to engineer novel antibodies against the checkpoint blockade target cytotoxic T lymphocyte associated protein 4 (CTLA-4) as tools to improve understanding of the anti-CTLA-4 mechanism of action against cancer. Although the first wave of antibodies made had favorable characteristics against CTLA-4 as a soluble target, they bound a CTLA-4 epitope too close to the cell surface and so could not be used for therapeutic studies. Next generation sequencing on the yeast libraries identified alternative CTLA-4 binding antibody sequences, and these will be tested in future mechanistic and therapeutic studies.
New Scientist magazine was launched in 1956 “for all those men and women who are interested in scientific discovery, and in its industrial, commercial and social consequences”. The brand’s mission is no different today - for its consumers, New Scientist reports, explores and interprets the results of human endeavour set in the context of society and culture.

An indexed directory of current research project abstracts in toxicology and related fields.

1038 references to research projects being conducted in the United States and elsewhere. Entries arranged under 5 topics, e.g., Preclinical studies of anticancer drugs, Preclinical radiation therapy, and Preclinical immunotherapy. Entries include title, researcher, address, contract number, summary, and supporting agency. Indexes by subjects, investigators, contractors, supporting agencies, and contractor numbers.

Focusing on deep conflicts between the medical establishment and the working class, Martha Balshem chronicles a health education project in “Tannerstown,” a pseudonym for a blue-collar neighborhood in northeast Philadelphia.

A new 300-bed regional hospital & cancer treatment centre is proposed for Abbotsford, British Columbia to replace the existing acute care portion of the Matsqui-Sumas-Abbotsford Hospital. This project will be the first complete major acute care hospital & cancer centre in the province developed through a public-private partnership project implementation process. This document invites interested parties to submit a written expression of interest (EOI) confirming their interest in participating in the hospital project, and demonstrating their capability, experience, expertise, capacity, & commitment to develop & operate infrastructure components of a hospital & cancer centre to world class standards. The document includes a project overview and information on the project scope, project implementation process & timetable, EOI submission requirements, EOI evaluation procedures & criteria, and general requirements of EOI respondents. Appendices include a site plan, a list of basic & optional facilities & services to be provided, a summary of facility requirements, and an EOI submission guideline.

Presents and assesses a variety of socio-cultural and behavioral factors that shape and influence lay and professional cancer prevention and control beliefs and actions.

*Summaries of papers* contained in the journal accompany each issue, 19--

Some volumes accompanied by addenda.

Rationale: Breast cancer is the most commonly diagnosed cancer, excluding skin cancers, and is the second leading cause of cancer death among women in the United States. Despite advancements in screening, early detection, and cancer treatments, not all women have benefited equally. Racial and ethnic minorities, particularly African American women, and those of low income have higher breast cancer mortality rates compared to the general population. Previous research has identified a number of demographic (e.g., race/ethnicity, age, health insurance, income), medical (e.g., comorbidities with other illnesses, family medical history), environmental (e.g., geographic area), and health system (e.g., type of cancer-related services available) factors associated with breast cancer disparities. However, these factors have largely been examined individually, and no study has comprehensively evaluated how multiple individual and contextual factors impact breast cancer outcomes. Therefore, this dissertation project had two primary aims: 1) to identify distinct subgroups of breast cancer patients based on demographic, medical, environmental, and health system factors that have been shown to influence timeliness of breast cancer care, and 2) to examine differences among emergent classes in timely initiation of breast cancer treatment. Design: The proposed study used archival data from the control arm of the Patient Navigation Research Project (PNRP), a five-year 10-site clinical trial of adult patients from medically underserved populations with an abnormal cancer screening or a new diagnosis of breast, cervical, colorectal, or prostate cancer. For this study, the sample included 198 patients with newly diagnosed Stage I-III breast cancer who received usual standard of care (control arm) from four PNRP sites, and who received a treatment for breast cancer (e.g., surgery, chemotherapy, radiation, hormonal therapy). Control participants were primarily recruited via medical record abstraction for which informed consent was waived. Exploratory Latent Class Analysis (LCA) was used to identify subgroups of breast cancer patients based on demographic (race/ethnicity, age at diagnosis, health insurance status, annual household income), medical (comorbidities [Charlson Comorbidity Index], family history of cancer), environmental (geographic residence [urban vs. rural], and health system (cancer-related services available onsite) factors associated with timeliness of breast cancer care. For the second aim, the study conducted logistic regression analyses to examine if class membership...
significantly predicted timely breast cancer treatment initiation, defined as initiation of any treatment for breast
cancer (e.g., surgery, chemotherapy, radiation, hormonal therapy) within 30 or 60 days of diagnosis, controlling for
type of breast cancer treatment. Results: Three classes of breast cancer patients were identified with varying patterns
of patient demographic, medical, and health system characteristics. The first class was distinguished by its high
endorsement of indicators associated with timely breast cancer care; patients in this class were most likely to be
White, have private health insurance, and have a family history of cancer. The second class was characterized by
individual and contextual factors associated with treatment delays, including having public health insurance, not
having a family history of cancer, and receiving care at a facility with the least amount of breast cancer services
available onsite. The third class represented breast cancer patients with the oldest average age at diagnosis and the
greatest number of medical comorbidities. Binomial logistic regression analyses demonstrated that the emergent
classes did not significantly differ in the likelihood of initiating breast cancer treatment within 30 days or 60 days
from breast cancer diagnosis, controlling for type of treatment. Conclusions: The present study used LCA to derive
classes of breast cancer patients based on simultaneous evaluation of demographic, medical, environmental, and
health system factors associated with timely breast cancer care. However, the emergent classes did not significantly
differ in terms of timely initiation of breast cancer treatment following definitive diagnosis of breast cancer. The
relatively small and homogenous study sample may have obscured differences in timeliness of breast cancer
treatment initiation. Future studies should utilize LCA with larger, more diverse samples of breast cancer patients to
identify distinct classes with unique combinations of individual and contextual characteristics that influence
timeliness of breast cancer care. Identification of distinct typologies of breast cancer patients provides a deeper
understanding of how the combination of factors synergistically impacts breast cancer outcomes and can help target
interventions to specific subgroups of patients that are most likely to experience delays in breast cancer care.