

# Inflammation and Cancer: human studies

1. There is convincing data that the amount and type of inflammatory infiltrate influences prognosis and possibly therapeutic responses in different types of human cancers, including, NSCLC, melanoma, colon ca, etc.
2. The lack of uniformity among these many studies renders the overall interpretation of the data difficult.
3. Moreover, the lack of comprehensive studies which have evaluated the presence and possible interactions among different types of immune cells, and among the immune cells and the tumor cells, renders the interpretation of these studies uncertain.

# Inflammation and Cancer: animal studies

- In rodents, especially in mice, it is possible to perform elegant studies to manipulate the immune system and study the biological significance of these altered immunological responses to different tumors.
- Although these studies have helped to understand the basic mechanisms of tumor immunology, their clinical-pathological significance remains to be assessed. This is because the pathogenesis of mice tumors is generally totally different than that of human tumors. This concept, that is well appreciated by physicians and surgical pathologists, needs to be taken into account by basic scientists to have meaningful investigations.
- Studies in mice can guide us to formulate hypotheses to perform studies in humans, but cannot be used to predict prognosis or responses to therapy in actual human patients.

# Inflammation and Cancer: What pathology can offer

- The information developed in animal models should always be evaluated in light of its potential clinical significance.
- Pathological evaluation allows us to validate the clinical significance of the results obtained in experimental models.
- The difficulty of performing mechanistic studies in humans should not discourage investigation in actual human tumor specimens, because this information is crucial to improve prognosis and/or treatment.

# Inflammation and Cancer: What pathology can offer

- There is a huge amount of specimens that is produced daily in each Department of Pathology that can be used to address clinical questions taking advantage of the new probes and technologies.
- We need to spend more time and resources studying human tumor specimens: this requires a change of attitude of study sections that presently fund only mechanistic experimental studies and label human studies as “descriptive and correlative”. Mechanisms are certainly important but unless we test their relevance in human models they remain an academic curiosity. In the past 2-3 decades we have developed a massive amount of mechanistic evidence, but this information so far has not had the desired effect on cancer prevention, diagnosis, prognosis or treatment.
- Clinical and Basic scientists need to work together, to sit in meetings together and they must sit together in study sections for a fair evaluation of grant applications with clinical emphasis.

# Inflammation and Cancer: what should be done

1. Perform comprehensive studies in human specimens evaluating in parallel the phenotype of the tumor cells (targets), the stroma, and the immune cells infiltrating the tumor microenvironment. Only a characterization of these components as a whole, in different types of malignancies, can provide information of clinical relevance, at least for some tumor types.
2. Such information is much needed at this present time to critically evaluate the potential significance of the massive amount of experimental data produced by immunologists in the past decade and to best plan how to go forward keeping the interest of the patients as our first priority.
3. These studies need to be standardized among pathologists working in different laboratories.
4. Precursor lesions and tumors at different stages and after different preventive or therapeutic interventions should be evaluated.
5. A significant and targeted NIH/NCI funding effort, to support a multi-laboratory study that will evaluate the immunophenotype of a large number of tumor biopsies of different histotypes, is required and it is strongly recommended.