Transforming pancreatic cancer from a death sentence into a treatable disease

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During the early development of cancer, many physiological processes occur in the vicinity of ‘young tumor cells’ that are similar to processes that occur during embryonic development and to healing of wounds in adult tissue, e.g., leukocyte recruitment and activation (inflammation), angiogenesis (development of new blood supply) and tissue remodeling. During tumor development; however, instead of initiating a 'healing' response, activated leukocytes provide growth-promoting factors that help tumors grow, in combination with factors that inhibit cytotoxic activities of CD8+ T cells. We are interested in understanding the molecular mechanisms that regulate leukocyte recruitment into neoplastic tissue and subsequent regulation those leukocytes exert on evolving cancer cells. To address these issues, we have taken several approaches to investigate mechanisms involved in: i. induction and maintenance of chronic inflammatory microenvironments in premalignant, malignant and metastatic tissues, ii. role of leukocyte in regulating tissue remodeling, angiogenesis, immune suppression and cancer development, and iii. development of novel non-invasive imaging reagents to monitor immune response in tissues/tumors. The long-term goal of this work is to translate basic observations made in the mouse, toward rational design of novel therapeutics whose aim will be to block and/or alter rate-limiting events critical for solid tumor growth, maintenance or recurrence in humans. Currently, we are actively utilizing transgenic mouse models of solid tumor development (non-small cell lung cancer, non-melanoma squamous and breast cancer, pancreatic adenocarcinoma, and mesothelioma) to reveal the functional roles of adaptive and innate leukocytes during tumor development, and to identify new targets for anti-cancer therapy. These experimental studies are conducted in parallel with evaluation of representative human cancer specimens to affirm that mechanisms revealed in the experimental setting represent fundamental parameters of multi-stage cancer development in humans.

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