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Application of cancer selective promoters for genetic-based imaging of metastasis and cancer therapy

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Our laboratory pioneered subtraction hybridization and used this elegant and effective gene identification strategy to clone novel genes of physiological relevance. Melanoma differentiation associated gene-7/interleukin-24 (mda-7/IL-24) was isolated from terminally differentiating human melanoma cells. mda-7/IL-24 is a novel member of the IL-10 gene family that promotes apoptosis and toxic autophagy in a broad-spectrum of human tumors, exerts potent bystander antitumor activity, inhibits tumor angiogenesis, stimulates the immune system and synergizes with conventional therapies (including chemotherapy, radiation, monoclonal antibodies and immuno-modulators) to promote selective tumor destruction. mda-7/IL-24 displays profound anti-cancer activity in preclinical animal models (including nude, syngeneic and transgenic mice) and following intra-tumoral administration using type 5 adenoviruses in a Phase I/II clinical trial in patients with advanced cancers. To enhance the therapeutic efficacy of mda-7/IL-24, we generated a novel class of adenoviruses, called cancer terminator viruses (CTVs), with enhanced tumor infectivity that selectively replicate in cancer cells and simultaneously produces mda-7/IL-24, Ad.5/3-CTV. Employing the same cancer-selective promoter used in the CTV, the rat progression elevated gene-3 promoter (PEG-Prom), we developed genetic-based imaging approaches for metastases. These approaches use the PEG-Prom (or another cancer-selective promoter) to drive an imaging gene (e.g., luciferase or HSV-Tk) linked to a delivery vehicle PEI. These nanoparticle vectors when combined with bioluminescence imaging and SPECT-CT permit non-invasive imaging of tumors and metastases in pre-clinical animal models. Using cancer-selective promoters, we have also generated mice which allowed the non-invasive imaging of tumor development, progression and therapeutic responses. Strategies are now being developed for theranostics in which tumors and metastases can be imaged and treated with a single vector. These theranostic vectors are being engineered in nanoparticles and in therapeutic CTVs. Overall, the novel reagents and methodologies, we have developed paradigm shifts in how cancers will be detected and treated in the future.

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Genomics - from revolt to revolution in the dairy cattle breeding industry

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The dairy industry has been changed forever as a result of the introduction Genomics. Not only from a science side, but also from how it has changed the economics of the dairy cattle breading industry. In dairy cattle industry we have had a phenotypic evaluation system for years for which we have been very aggressive in how we can use genomics and the development of snippets to determine early in life the potential of an animal, greatly increasing the reliability of our breeding predictions. Though this we have changed the industry drastically over the past 5 years. The whole economics of the dairy breeding industry are different. It has eliminated the seed stock producer and been replaced by larger breeding organizations. It has also changed how the typical commercial producer views their investment in genetics. No longer is it a commodity purchase, the greatly increased reliabilities has encouraged producers to invest in higher and more expensive genetics. As a result of these changes the rate of genetic gain has increased almost five times in the past five years. Now on the verge of technologies like gene the rate of genetic gain is only going to accelerate that much faster.

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