Seminar: Wednesday the 10th of December 13:15-14:30 in 8W 2.1

UNIVERSITY OF BATH

Immunosenescence and cancer

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Abstract

Numerous data from mouse models firmly support the notion of immunosurveillance of cancer proposed many years ago but remaining controversial until quite recently. Moreover, the clear clinical benefits of boosting anti-tumor immune responses by therapeutic vaccination now being reported, and especially the dramatic results of treatment with immune checkpoint modulators in different tumor types, are unequivocally documenting the power of immunity to control cancer. In most animal models and in clinical experience, it is the adaptive arm of immunity, especially the T cells, which are most important in this respect. However, it is appreciated that immunity wanes with age. An unanswered question is to what extent this impacts on immunosurveillance and immunotherapy of cancer. Most mouse models use young animals, but where investigators have on occasion examined the same therapeutic protocols in old animals, the results have always been different, usually worse, than in the young. Most solid tumors in humans are age-associated diseases, raising the question of whether immunosenescence compromises not only responses to infectious agents but also to cancer. There are few data available thus far in this respect. In elderly people without overt cancer, changes associated with immunosenescence are now known to be exacerbated by exposure to chronic antigenic stress throughout life. In the first instance, this “immune exhaustion” is a result of unbalanced hematopoiesis generating altered proportions of immune cells, and to thymic involution early in life severely curtailing the generation of fresh supplies of naïve T cells. Thus, the individual must go through life with relatively fixed amounts of immune resources which are called upon to defend against repetitive acute infections, but most importantly, to maintain the immunosurveillance we know is required to control persistent infections, especially viral infections, and most notably with the essentially ubiquitous herpesvirus, Cytomegalovirus (CMV). This latent virus, like many tumors, constantly interacts with the immune system, cannot be rejected, and results in signs of immune exhaustion. The collateral damage resulting from such immunosurveillance includes the increased detrimental background inflammatory status seen in most older people and animals (dubbed “inflammaging”) which may itself be pro-carcinogenic. This presentation will explore the possibility that tumor antigens and CMV antigens in humans may induce similar senescent changes in T cells, how these may be manipulated to improve immune function, and whether the potentially deleterious effects of CMV together with tumor antigens in cancer patients may be additive.

Hosted by Dr James Turner, Department for Health.
Please contact j.e.turner@bath.ac.uk if you would like to meet with Graham after the seminar.