Neoplasia (basic science)

**PMO-088**
A LARGE PROPORTION OF COLORECTAL TUMOUR-INFILTRATING CD4+ T CELLS ARE SUPPRESSIVE IRRESPECTIVE OF FOXP3 EXPRESSION
doi:10.1136/gutjnl-2012-302514b.88

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**Introduction** The presence of increased numbers of CD3+ T cells in colorectal cancer (CRC) correlates with improved prognosis. However, it is difficult to measure anti-tumour responses in tumour-infiltrating lymphocytes (TILs) suggesting these cells are suppressed. Although we have demonstrated CD4+Foxp3+ regulatory T cells (Tregs) within the tumour and its stroma, the numbers are often low. We sought to identify phenotypic and functional characteristics of CD4+Foxp3+ T cells to determine whether other regulatory populations exist within this environment.

**Methods** Tumour samples were obtained from CRC patients with different stages of malignancy. Fixed tumour samples were examined by immunofluorescence and CD3, CD8 and FoxP3. TILs from fresh tumour tissue were stained with a panel of 20 antibodies (including Helios, LAG-3, LAP) and examined by FACS.

**Results** Histology revealed tumours to be infiltrated by CD4+, CD8+ and Foxp3+ positive cells. Despite an increase in CD4+ and CD8+ T cells in advanced tumours, there was not always a concomitant increase in Foxp3+ cells. Flow cytometry revealed the majority of the Treg fraction was Helios+ (indicating thymically-derived) and expressed higher levels of CTLA-4 and CD39 than Tregs from colon and blood. However, 30% of “conventional” CD4+Foxp3+ T cells express markers associated with Tregs including LAP (latency-associated peptide), LAG-3 and CD25 and were highly suppressive in vitro.

**Conclusion** Tumour-infiltrating CD4+ T cells are heterogeneous. A high percentage of these cells appear to have a regulatory function and include both Foxp3+ as well as FoxP3- T cells. Overcoming the suppressive environment of CRC is a major challenge for boosting anti-tumour immunity.

Competing interests None declared.

**REFERENCES**