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Shaping the macrophage landscape in the tumour microenvironment

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Tumour-associated macrophages (TAMs) are key orchestrators of the immune and stromal microenvironment, affecting cancer progression, metastatic ability, and the tissue's inflammatory balance. In this issue of the *Central European Journal of Immunology* (CEJI), Lu *et al.* report that colorectal cancer (CRC)-derived LAMA1 promotes macrophage M2 polarisation by activating the EGFR–AKT–CREB pathway. Their study offers a new mechanistic understanding of how tumour-derived extracellular matrix (ECM) components can influence macrophage function and, in turn, the tumour microenvironment (TME) [1].

While cytokines and soluble mediators have long been recognised as orchestrators of macrophage phenotype, Lu *et al.* expand this understanding by demonstrating that a basement membrane component, namely LAMA1, can serve as a signalling mediator rather than solely as a structural component. Identifying the EGFR–AKT–CREB pathway as an intracellular signalling pathway regulating macrophages enhances our understanding of how tumour cells may indirectly influence immune responses [1].

This research aligns with a broader trend observed in CEJI publications over the past 2 years, where several studies have explored macrophage plasticity and the complex dialogue between the tumour and immune compartments.

For instance, Huang *et al.* demonstrated that exposure to the anaesthetic sevoflurane alters macrophage-like cell polarisation in a cervical-cancer model [2]. Similar findings have been reported for lung adenocarcinoma, where ANKRD22 expression facilitated angiogenesis by skewing macrophage-like cells' activation states [3]. Collectively, these studies, and now the contribution by Lu *et al.*, as well as recently published reports in other journals, emphasise that a single pathway does not govern TAM polarisation but results from the integration of multiple environmental and molecular signals [4, 5]. From a scientific standpoint, the study reinforces a crucial message: macrophages interpret not only cytokine gradients, but also structural and biochemical cues derived from the ECM [6, 7]. This recognition broadens our understanding of immune regulation within tumours, positioning the ECM as an active participant in shaping immune cell function [8].

Taken together, the work by Lu *et al.* adds a valuable layer to the evolving narrative of macrophage biology in cancers [1]. By uncovering a previously unappreciated ECM-to-macrophage signalling route, this study enriches our mechanistic understanding of tumour–immune crosstalk. It highlights the ongoing need for experimental systems that bridge models with physiological complexity.

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