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Inhibition of MYC in macrophages: tumor vs inflammation-related diseases

Emilio Cano-Ramos[1], Begoña Lavin[2], and Oscar M Pello[1,*]
[1]Imperial College London; [2]King's College London

Inhibition of MYC has been postulated as one of the most promising anti-tumoral therapies. However, if some anti-inflammatory cells express MYC, would an anti-tumoral treatment targeting MYC facilitate subsequent inflammation-related disorders?

Inhibition of MYC expression/activity using chemical inhibitors, anti-sense oligonoucleotides or RNA interference has been postulated as one of the most promising antitumor therapies.[1] Within the tumor mass, cancer cells, as well as other components of the microenviroment such as tumor-associated macrophages (TAMs), can express the potent, growth promoting transcription factor MYC.[2,3] It would be interesting to know whether other cells within the tumor (e.g. lymphocytes and other immune cells, fibroblasts, mesenchymal stem cells, etc) are also able to express MYC and whether the antitumor efficiency of anti-MYC drugs is partially due to their effects on these tumor-related cells. In this regard, we recently described that inhibiting MYC only in the myeloid compartment in mice reduces melanoma and fibrosarcoma tumor growth.[4,5]

TAMs are generally considered "alternatively activated", M2 or M2-like macrophages, a group which refers to all macrophage subtypes which are activated by stimuli different from T helper type 1 (Th1) inflammatory cytokines, showing a specific phenotype and exerting particular functional activities.[6] Among these, the anti-inflammatory properties of M2 macrophages are needed to avoid exacerbated inflammatory responses and inflammation-related pathologies.[6]

Interestingly, mice lacking MYC in myeloid cells show a normal immune system in steady-state conditions compared to control littermates.[4,5] However, in response to an inflammatory stimulus like aortic denudation, these animals are less able to clear and resolve inflammation, which persists for an extended period of time.[7]

Although the role of MYC in fully differentiated immune cells has only recently began to be elucidated in detail, assuming that M2 macrophages and other anti-inflammatory cells express MYC,[2,8,9] would an antitumor treatment targeting MYC facilitate subsequent inflammation-related disorders? Although this "secondary effect" has not been evaluated in the majority of published studies targeting MYC for tumor therapeutic purposes, some reports have pointed to the possibility that MYC blockade may elicit undesirable inflammatory reactions.[10,11] In order to optimize future MYC-targeting antitumor treatments in the clinic, we believe that monitoring the resulting inflammatory status of pre-clinical antitumor models targeting MYC expression or activity is necessary to avoid or minimize unexpected inflammatory complications in treated patients.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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*Correspondence to: Oscar M. Pello, PhD John Goldman Centre for Cellular Therapy, Department of Hematology, Hammersmith Hospital, Imperial College Healthcare NHS Trust. 150 Du-Cane Road, London W12 0HS; Email: o.pello@imperial.ac.uk

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