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VABILO

Nacionalni inštitut za biologijo Vas vabi, da se udeležite seminarja

»Using cellular neighbourhoods to identify therapeutic strategies in non-small cell lung cancer«,

ki ga bo predstavila

dr. Febe van Maldegem

Vodja laboratorija za imunologijo pljučnega raka, Amsterdam University Medical Centres

Seminar bo v torek, 19. septembra 2023, ob 13.30 uri

v Biološkem središču, Večna pot 111, v Ljubljani, v predavalnici B5 in preko ZOOM povezave:

https://us02web.zoom.us/j/86925602351?pwd=LzdmamR0RWRrTkhNRER2ZUFKZ2F1dz09

Meeting ID: 869 2560 2351, Passcode: 058686

Povzetek v angleškem jeziku

The recent development and approval of KRAS-G12C inhibitors promises to change profoundly the clinical management of lung cancer patients harbouring KRAS-G12C mutations. However, early clinical data indicate that acquired drug resistance can frequently develop after the initial response. Due to the immunosuppressive nature of the signalling network controlled by oncogenic KRAS, targeted KRAS-G12C inhibition can indirectly affect anti-tumour immunity. We characterised how KRAS-G12C inhibition leads to reduced infiltration of immunosuppressive cells and enhanced infiltration and activation of cytotoxic T cells. However, the combination of KRAS-G12C inhibitors with immune checkpoint blockade only provides synergistic benefit in the most immunogenic tumour models. To investigate mechanisms that restrain immunotherapy sensitivity in non-responsive tumours, we used multiplex imaging mass cytometry to explore spatial patterns in the tumour microenvironment. We identified a community harbouring features of localised T-cell activation, where CD4 and CD8 T cells and dendritic cells were gathered together. KRAS-G12C inhibition led to increased expression of PD-1 on T cells, closer proximity of T cells to dendritic cells within this community, together with increased proliferation and potential cytotoxicity of CD8+ T cells, indicating an effector response. However, we also observed a high incidence of regulatory T cells (Tregs) within this community, suggesting that these were dampening the anti-tumoural immune responses following KRAS-G12C inhibition. Depleting Tregs in vivo rescued the anti-tumour immune response and led to enhanced tumour control in combination with anti-PD1 and KRAS-G12C inhibitor. We therefore propose KRAS-G12C inhibitor combination with Treg depletion as a therapeutic opportunity to achieve durable responses.

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Vljudno vabljeni! Seminar bo potekal v angleškem jeziku. / **You are cordially invited to attend this lecture, which will be delivered in English.**

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