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Long-lasting alterations in lung anti-tumor immunity by viral infections

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Respiratory viruses are among the most common infectious agents in humans. Beyond their pathogenic characteristics, viruses have the potential to induce lasting alterations in host immunity. These virus-induced changes have been shown to modulate immune responses to heterologous infections and to affect susceptibility to the development of allergic asthma. However, the consequences of respiratory viral infections on the development of effective anti-tumor responses are still unkown.

To investigate whether changes imprinted by different viruses could affect tumor implantation and progression, we used a murine model of Lewis lung carcinoma and two different viruses: Murid herpesvirus 4 (MuHV-4) and Pneumonia virus of mice (PVM), which are homologs of two widely distributed human viruses, Epstein-Barr virus and respiratory syncytial virus, respectively.

Our results show that infection with MuHV-4 or PVM has an opposite effect on lung tumor development. While MuHV-4 infection impairs tumor establishment, PVM infection promotes engraftment and tumor growth. Interestingly, MuHV-4 infection triggers a potent Th1 and CD8 effector T cell response that correlates with the presence of polarized ‘M1-regulatory’ alveolar macrophages, suggesting a key crosstalk between these cellular players. Conversely, PVM infection results in defective Th1 and CD8 effector T cell responses. This anergic state correlates with the accumulation of immunosuppressive myeloid cells, including 'M2-like' alveolar macrophages, which may have a permissive influence on tumor development.

Overall, our work highlights that the specific history of infections can have unexpected long-term consequences that profoundly shape anti-tumor immune responses.