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QUIESCENT EPITHELIAL STEM CELLS EVADE IMMUNE SURVEILLANCE

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There is a long-standing interest in understanding the immunogenicity of adult stem cells due to their role in tissue homeostasis, regeneration and oncogenesis. Notably, their self-renewing capacity means they are long-lived, and can accumulate mutations over time, which would result in neo-antigens. These neoantigens could make stem cells potential targets of T cells. However, whether they are subject to immune surveillance is unknown. Here, we utilized a novel technology to study immune responses against virtually any cell type, along with specific stem cell mouse models, to interrogate the immunogenicity of adult stem cells in their niche *in vivo*. We found that immune privilege is not a general property of adult stem cells. Instead, our studies revealed that most epithelial stem cells, such as those in the gut and ovary are subject to immune clearance, but that highly quiescent stem cells, specifically in the skin and muscle, escape immune detection. This is an intrinsic property of the resting stem cells resulting from downregulation of MHC class I and other key components of the antigen presentation machinery, which results in complete protection from immune attack. These studies established that quiescent tissue stem cells hide from immune surveillance and protect their integrity. This helps to understand why mutations in long-lived stem cells do not lead to immune clearance and, suggests how cancer stem cells may evade immune surveillance.

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