**Leveraging epigenetic regulation of stemness for basal cell carcinoma immunoprevention**

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Keratinocyte carcinoma (KC), including basal cell carcinoma (BCC) and cutaneous squamous cell carcinoma (cSCC), is the most common cancer with a continuous rise in incidence. Despite harboring the highest tumor mutational burden of all cancers, BCC has low immunogenicity. Herein, we demonstrate that BCC’s low immunogenicity results from epigenetic suppression of antigen presentation machinery reminiscent of its cell of origin. Primary BCC had low immune cell infiltrates and lacked human leukocyte antigen class I (HLA-I) expression compared with cSCC and normal keratinocytes. Forkhead box C1 (Foxc1), a regulator of quiescence in hair follicle stem cells, was expressed in BCC. Foxc1 bound to promoter of interferon regulatory factor 1 and HLA-I genes leading to their deacetylation and reduced expression. A histone deacetylation inhibitor, entinostat, overcame Foxc1’s effect by inducing acetylation and upregulated HLA-I in BCC. Entinostat upregulated β-2 microglobulin expression in BCC *in vivo*. Topical entinostat plus imiquimod immunotherapy prevented BCC development in mice. Collectively, our findings demonstrate that low BCC immunogenicity originates from the stem-like quiescent program preserved in the tumor cells, which can be blocked by entinostat to enable BCC immunotherapy.