

Table S1. Regulatory role of the COX-2/Prostaglandin E2 pathway of the immunoediting mechanism in cancer development.

Target	Effects of COX-2 and PGE2	References
CDA4+ and CD8+T cells	-PGE2 inhibits production and proliferation -PGE2 promotes differentiation in Treg	[84,85]
Th1	-PGE2 inhibits TH1 proliferation	[86]
Treg	-COX-2 expression regulates Treg induction -COX-2 via Treg inhibits Th1 activation -COX-2 inhibition attenuates Treg activation	[87–90]
NK	-PGE2 inhibits migration, cytotoxic effects and secretion of IFN-gamma. -COX-2 inhibitors re-establish NK functions	[93–98]
DC	-PGE2 suppress tumor-infiltrating DC activation -PGE2 promotes differentiation DC into monocytic MDSC and facilitates immune evasion -PGE2 enhances IL-10 production and down-regulates DC functions -PGE2 inhibits secretion of IFN-alpha which results in the induction of Th2 cytokines and reduction of Th1 cytokines	[99–104]
Macrophages	-COX-2 inhibition shifts the phenotype of TAM from M2 to M1	[106]
MDSCs	-COX-2 inhibition prevents local and systemic expansion -PGE2 maintains the suppressive activity of cells	[108–113]
Angiogenesis	-Overexpression of COX-2 induces production of VEGF -PGE2 stimulates VEGF expression	[115–119]
Wnt/Beta-Catenin pathway	-COX-inhibition attenuates signalling transmission -COX-2 inhibition and antagonist of EP2 and EP4	[144]
Exosomes	receptors attenuates the inhibitory effects of exosomes over NK cytotoxic activity	[142]

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