Key Messages

- We identified novel interactions of extracellular REIC/Dkk-3 with cell surface C5aR, CXCR2, CXCR6, and CMTM6 (in addition to CXCR7, which was already known as one of the potent REIC/Dkk-3 receptors).
- REIC/Dkk-3 regulates an immune checkpoint via an acceleration of PD-L1 collapse through the interaction with the identified receptors.
- The downregulation of PD-L1 evoked by REIC/Dkk-3 associates with a dampened cancer growth in vivo at significant level.