Site-Specific Immunomodulators exploit the potent immune response to infection to effectively mobilize innate anti-tumour immunity

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Clinical application of the relationship between infection and cancer inhibition was documented on papyrus from Iberia dating back to 1550 BC. Dr. William Coley brought this insight to Western Medicine in the late 1800’s when he noted spontaneous tumor remission in some patients experiencing acute infections. Optimal use of microbial immunotherapeutic strategies has been hampered by poor understanding of their bases. Qu Biologics, a clinical stage biotechnology company, has discovered a means to target the immunological mechanisms that underlie this phenomenon. Repeated subcutaneous injections of Site-Specific Immunomodulators (SSIs), made from pathogens known to commonly cause infection in a particular organ or tissue, show efficacy in treating cancers growing in the targeted organ (Figure 1).

Figure 1. SSIs stimulate immune function in the targeted organ or tissue

RESULTS

Figure 2. SSIs show site specificity for the treatment of cancer

(A) Lung tumour nodule counts at day 18 in animals obtained from facilities positive for Klebsiella or negative for Klebsiella administered placebo or QBKPN.

(B) Lung tumour nodule counts in mice pre-infected with Streptococcus pneumoniae or Pseudomonas aeruginosa and administered SP (derived from S. pneumoniae) or Pseudomonas-derived immunotherapy (PA).

Mean ±/− SD, n = 4−8 mice / group. *P < 0.05, **P < 0.01, ****P < 0.0001 by 1-way ANOVA followed by Tukey’s multiple comparison test.

Figure 3. QBKPN anti-tumour efficacy requires host exposure to lung microbe, Klebsiella

(A) Proportion of immune cells in the lungs of mice with lung cancer, given placebo or QBKPN. Upper pie charts show the proportion of B cells, T cells, NK cells, and myeloid cells. Lower pie charts: proportion of different myeloid cells. (B) Pathological changes in the lungs of mice administered with QBKPN or placebo. (C) NKG2D ligand expression on tumour cells of mice administered with QBKPN or placebo.

Mean ±/− SD, n = 8−10 mice / group. *P < 0.05; **P < 0.01; ***P < 0.001 by Student’s t-test.

Figure 4. Adaptive Immunity is dispensable for QBKPN anti-tumour efficacy

(A) Lung tumour nodule counts of mice with or without CD25+ cell depletion, after administration of placebo or QBKPN. (B) Lung tumour nodule counts of mice with or without CD4+ cell depletion, after administration of placebo or QBKPN.

Mean ±/− SD, n = 4−5 mice / group. *P < 0.05; **P < 0.01 by Student’s t-test.

DISCUSSION AND CONCLUSIONS

Treatment with a lung directed SSI, QBKPN, provided a safe and effective method to mimic an acute infection leading to significantly reduced lung tumour burden and increased survival. QBKPN efficacy was driven largely by innate immune mechanisms including a marked increase in the number of phagocytic leukocytes in circulation, shift in monocyte polarization to M1 dominance in the organ, up-regulation of NKG2D ligands on tumour cells, and enhanced cytotoxic lymphocyte activity. Blocking adaptive immune function, using depleting antibodies against T cell subsets or Rag2 knockout mice, did not alter QBKPN efficacy. SSIs’ targeted anti-tumour effects were replicated in colon and skin cancer models. In collaboration with the BC Cancer Agency, a Phase I clinical trial in patients with non-small cell lung cancer confirmed the safety and tolerability of this innovative cancer immunotherapy strategy.