

Yeast-based immunotherapy for cancer – Engineering sheep in wolf's clothing

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The administration of targeted molecular immunogens (a.k.a. TarmogensTM), which are whole, heat-inactivated *S. cerevisiae* yeast containing defined quantities of target antigens, elicit T cell-mediated immune responses that eliminate antigen-bearing diseased cells. Yeast are innately taken up via pattern recognition receptors, including multiple TLRs, on dendritic cells (DCs). This innate immune response drives DC maturation, secretion of pro-inflammatory cytokines and MHC-mediated presentation of yeast-expressed disease antigens for antigen-specific immune responses. Attractive features of the Tarmogen approach include its broad applicability to multiple disease targets, the speed of development from concept to the clinic, and its scalability to support clinical and commercial production. Preclinical data of the immunogenicity and efficacy of administering yeast expressing mutated Ras proteins (GI-4000), CEA (GI-6000) and targeting imatinib (Gleevec) resistance escape mutants in CML will be presented. The tolerability and immunogenicity of administering mutant Ras-expressing (GI-4000) Tarmogens in a Phase 1 trial treating advanced cancer patients will be described. Because of the results from the Phase 1 study, a multi-center, placebo controlled double blind Phase 2 trial with GI-4000 has been initiated for the treatment of patients with pancreas cancer. In summary, the delivery of target antigens by yeast triggers innate immunity and elicits protective antigen-specific immune responses for the treatment of cancer.