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Methods and Compositions of Using Peroxiredoxin 1 (Prx1) as an Adjuvant

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Keywords: Peroxiredoxin 1 (Prx1), immunotherapy, vaccine, chaperone, adjuvant, multimer, toll like receptor 4 (TLR4), CpG motif.

Collaboration Research Opportunity: Roswell Park Cancer Institute is seeking partners to help co-develop use of Peroxiredoxin1 as an adjuvant stimulating an immune response for therapeutic and prophylactic treatment of cancer.

Summary: The antioxidant Peroxiredoxin 1 (Prx1) is a molecular chaperone that acts as a regulator of hydrogen peroxide signaling, is overexpressed in many cancers, and is often secreted from tumor cells. Prx1 expression is elevated in various cancers, including esophageal, pancreatic, lung, follicular thyroid, and oral cancer. Elevated Prx1 levels have been linked with poor clinical outcomes and diminished overall patient survival. Recent studies have also shown that Prx1 can be secreted by non-small cell lung cancer cells. The function of secreted Prx1 is unknown and has not been previously exploited for therapeutic purposes.

Technology: Researchers at the Roswell Park Cancer Institute have demonstrated that the inclusion of Prx1 with a vaccination to tumor antigens elicited macrophages or immature bone marrow-derived dendritic cells resulted in TLR4-dependent secretion of TNF-α and IL-6 and dendritic cell maturation leading to a more robust immune response.

Like other chaperone proteins and molecules involved in the innate immune response, PRrx1 is thought to play a role in the elicitation of robust, adaptive immune responses. The addition of Prx1 as a component of the vaccine adjuvant resulted in a marked increase in tumor free survival in a mouse model compared to a vaccine/adjuvant lacking Prx1.

Vaccinating against tumor antigens has thus far proven to not be a robust strategy for treating/preventing cancer. While there may be a multitude of reasons that this once-promising strategy has not worked, there is a belief that a priming of the innate immune system may be needed or helpful to elicit sustained immune response.

Potential Commercial Applications:

- Stimulated immune response can have a therapeutic or prophylactic effect and can include a cell-mediated and/or humoral response or a combination of both.
- Prx1 exhibits many of the same activities as CpG and imiquimod, however receptor to which it binds, TLR4, is more broadly expressed than TLRs that interact with CpG and imiquimod. Thus, Prx1 has potential to be a more effective anti-cancer vaccine adjuvant.
- This invention can be used to stimulate an immune response to *any* antigen, and thus the antigen will function as an immunogen.

Competitive Advantages:

- Vaccination with adjuvants containing peroxiredoxin could provide a more robust strategy for vaccination against tumor antigens.
- Addition of Prx1 to an anti-tumor vaccine may increase the potency of the vaccine.
- It may be useful to combine this strategy with other vaccination therapies targeted to tumor antigens (survivin, PD-1, CA-125).

Development Status: Patent Status: US 2011/0177129 PCT/US2010/059411, PCT - South Korea, China, Canada, India

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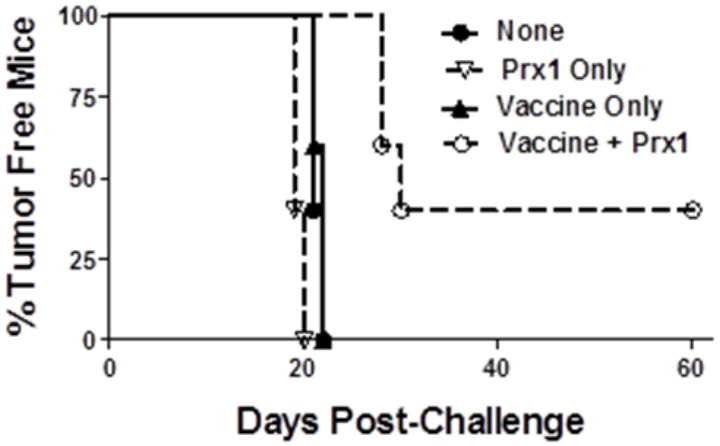

Figure 1: Prx1 Augments Anti-Tumor Vaccine Efficacy. Naïve mice were vaccinated with whole cell tumor lysate alone or in combination with 20nM recombinant Prx1. After 1 week of rest, mice were challenged by injection of live tumor cells. Tumor growth was monitored for 60 days; n=10 mice/group