PDT-Induced Immunity

The ideal cancer treatment should target both the primary tumor and the metastases with minimal toxicity. This is best accomplished by educating the body's immune system to recognize the tumor as foreign so that after the primary tumor is destroyed, distant metastases will also be eradicated. PDT may accomplish this feat and stimulate long-term, specific anti-tumor immunity. PDT causes an acute inflammatory response, the rapid induction of large amounts of necrotic and apoptotic tumor cells, induction of immunostimulatory heat-shock proteins, tumor antigen presentation to naïve T-cells, and generation of cytotoxic T-cells that can destroy distant tumor metastases.

By using various syngeneic mouse tumors in immunocompetent mice, we can study specific PDT regimens related to tumor type as well as mouse genotype and phenotype. We have investigated the role of tumor-associated antigens in PDT-induced immune response by choosing mouse tumors that express: model defined antigen, naturally-occurring cancer testis antigen, and oncogenic virus-derived antigen.

We studied the synergistic combination of low-dose cyclophosphamide and PDT that unmasks the PDT-induced immune response by depleting the immunosuppressive T-regulatory cells. PDT combined with immunostimulants (toll-like receptor ligands) can synergistically maximize the generation of anti-tumor immunity by activating dendritic cells and switching immunosuppressive macrophages to a tumor rejection phenotype. Tumors expressing defined tumor-associated antigens with known MHC class I peptides allows anti-tumor immunity to be quantitatively compared.



Related Publications

Castano AP, Gad F, Zahra T, Hamblin MR. Specific anti-tumor immune response with photodynamic therapy mediated by benzoporphyrin derivative and chlorin(e6). Proc SPIE; 2003, Vol 4612: p 1-9 Castano AP and Hamblin MR. Anti-tumor immunity generated by photodynamic therapy in a metastatic murine tumor model. Proc SPIE, 2005; Vol 5695:p 7-16.

Castano AP and Hamblin MR. Enhancing photodynamic therapy of a metastatic mouse breast cancer by immune stimulation. Proc SPIE, 2006; Vol 6087. art. no. 608703.

Hamblin MR, Castano AP and Mroz P. Combination immunotherapy and photodynamic therapy for cancer. Proc SPIE; 2006; Vol 6087. art. no. 608702.

Castano AP, Liu Q, and Hamblin MR. Green fluorescent protein expressing but not wild-type tumors in mice are cured by photodynamic therapy. Brit J Cancer, 2006, 94, 391-397.

Castano AP, Mroz P, and Hamblin MR. Photodynamic therapy and anti-tumour immunity. Nat Rev Cancer, 2006, 6: 535-545

Mroz P, Castano AP. Wu MX, Kung AL, Hamblin MR. Photodynamic therapy stimulates anti-tumor immunity in murine models. Proc SPIE 6438. 2007; DOI: 10.1117/12. 697630.

Mroz P, Hamblin MR. Photodynamic therapy stimulates anti-tumor immunity in a murine mastocytoma model. In: Chen WR, Editor; Biophotonics and Immune Responses III, Bellingham, WA, The International Society for Optical Engineering, Proc SPIE 6847, 2008.

Castano AP, Mroz P, Wu MX, Hamblin MR. Photodynamic therapy plus low-dose cyclophosphamide generates antitumor immunity in a mouse model. Proc Natl Acad Sci USA, 2008,105(14):5495-5500.

Mroz P, Castano AP, Hamblin MR. Stimulation of dendritic cells enhances immune response after photodynamic therapy. Proc SPIE 2009 in press

Szokalska A, Makowski M, Nowis D, Wilczynski GM, Kujawa M, Wójcik C, Mlynarczuk-Biały I, Salwa P, Bil J, Janowska S, Agostinis P, Verfaillie T, Bugajski M, Gietka J, Issat T, Glodkowska E, Mrówka P, Stoklosa T, Hamblin MR, Mróz P, Jakóbisiak M, Golab J. Proteasome inhibition potentiates antitumor effects of photodynamic therapy in mice through induction of ER stress and unfolded protein response. Cancer Res. 2009. 69(10):4235-43.

Mroz P, Szokalska A, Wu MX, Hamblin MR. Photodynamic Therapy of Tumors Can Lead to Development of Systemic Antigen-Specific Immune Response. PLoS ONE, 2010, 5 (12), e15194-05

Mroz P. Hashmi JT, Huang YY, Lange N, Hamblin MR. Stimulation of anti-tumor immunity by photodynamic therapy. Expert Rev Clin Immunol, 2011. 7(1): p. 75-91.

Mroz P, Hamblin MR. The immunosuppressive side of PDT. Photochem Photobiol Sci, 2011, 10(5):751-8.

St. Denis TG, Aziz K, Waheed AA, Huang YY, Sharma SK, Mroz P, Hamblin MR. Combination approaches to potentiate immune response after photodynamic therapy for cancer. Photochem Photobiol Sci, 2011, 10(5):792-801.

Mroz P, Yaroslavsky A, Kharkwal GB, Hamblin MR. Cell Death Pathways in Photodynamic Therapy of Cancer. Cancers 2011, 3, 2516-2539.

Research Projects

- Photodynamic inactivation of pathogens
- Antimicrobial PDT for localized infections
- PDT-induced anti-tumor immunity
- Mechanistic studies of new bacteriochlorin and fullerene photosensitizers
- Mechanisms of low-level light therapy
- Low-level light therapy for traumatic brain injury
- Blue-light therapy for infections
- Ultraviolet C therapy for localized infections
- Wound Healing and Infection
- Macrophage-targeted PDT
- Detection and therapy of vulnerable atherosclerotic plaque

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