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Ph.D., Roswell Park Cancer Institute Graduate Division, State University of New York at Buffalo, 2005

Molecular Immunology; MHC-associated antigen processing machinery; NK cell biology

Research Interests

Why do tumors grow in spite of a competent host immune system? Do cancer cells develop strategies to evade host tumor-specific immune responses? How are the gene products of *MHC*, or major histocompatibility complex, and components of antigen processing machinery manipulated by malignant cells? How does intrinsic genotoxic stress contribute to NKG2D-related innate self/non-self discrimination imbalance, which promotes cancer immune surveillance and escape? These interesting and fundamental questions are addressed at the molecular level in the Chang Laboratory using a number of state-of-the-art cellular, molecular biological, biochemical and structural biological approaches.

Recent Publications

1. Hsieh, C.-H., Hsu, Y.-J., **Chang, C.-C.**, Liu, H.-C., Chuang, K.-L., Chuang, C.-K., Pang, S.-T., Hasumi, K., Ferrone, S., and Liao, S.-K. (2008). Total HLA class I loss in a sarcomatoid renal cell carcinoma cell line caused by the coexistence of distinct mutations in the two encoding β2-microglobulin gene. Cancer Immunol. Immunother. [Epub ahead of print] DOI: 10.1007/s00262-008-0565-7
2. **Chang, C.-C.**, Pirozzi, G., Errico, S., Luongo, M., Lombardi, M.L., and Ferrone, S. (2008). Combination of germline and somatic TAPBP gene mutations, HLA haplotype loss and epigenetic silencing of HLA-A gene responsiveness to IFN-g in melanoma cells with HLA class I downregulation. Cancer Res., in revision.
3. Wongsena, W, Sconocchia, G, Cho H.-S., **Chang, C.-C.**, Wang, X., Klumkrathok, K., Ferrone, S., and Leelayuwat, C. (2008) Production and characterization of monoclonal antibodies against major histocompatibility complex class I chain-related gene A. Tissue Antigens. 72:431-440.
4. Sangrouber, D., Marcou, C., Le Discorde, M., **Chang, C.-C.**, Carosella, E.D., and Moreau, P. (2007). Cellular co-localization of intron-4 containing mRNA and HLA-G soluble protein in melanoma analyzed by fluorescence in situ hybridization. J. Immunol. Methods 326, 54-62.
5. **Chang, C.-C.,** and Ferrone, S. (2007). Immune selective pressure and HLA class I antigen defects in malignant lesions. Cancer Immunol. Immunother. 56, 227-236.
6. **Chang, C.-C.,** and Ferrone, S. (2006). NK cell activating ligands on human malignant cells: molecular and functional defects and potential clinical relevance. Semin. Cancer

Biol. 16, 383-392.

7. **Chang, C.-C.**, Ogino, T, Mullin, D.W., Yamshchikov, G.V., Bandoh N., Slingluff, C.L. Jr., and Ferrone, S. (2006). Defective HLA class I-associated antigen presentation caused by a novel β_2-microglobulin loss-of-function in melanoma cells. J. Biol. Chem. 281, 18763-18773.
8. Shen, C., **Chang, C.-C.**, Zhang, J., Guo, W., Xia, L., Meng, F., and Xie, W. (2006). Structural and functional characterization of peptide-β_2m fused HLA-A2/MART127-35 complexes. Biochem. Biophys. Res. Commun. 342, 57-65.
9. **Chang, C.-C.**, Hernandez-Guzman, F.G., Luo, W., Wang, X., Ferrone, S., and Ghosh, D. (2005). Structural basis of antigen mimicry in a clinically relevant melanoma antigen system. J. Biol. Chem. 280, 41546-41552.
10. Yan, W.-H., Lin, A.-F., **Chang, C.-C.**, and Ferrone, S. (2005). Induction of HLA-G expression in a melanoma cell line OCM-1A following the treatment with 5-aza-2'-deoxycytidine. Cell Res. 15, 523-531.
11. Yamshchikov, G.V., Mullins, D.W., **Chang, C.-C.**, Ogino, T., Thompson, L., Presley, J., Galavotti, H., Aquila, W., Deacon, D., Ross, W., Patterson, J.W., Engelhard, V.H., Ferrone, S., and Slingluff, C.L., Jr. (2005). Sequential immune escape and shifting of T cell responses in a long-term survivor of melanoma. J. Immunol. 174, 6863-6871.
12. **Chang, C.-C.**, Campoli, M., and Ferrone, S. (2005). Classical and non-classical HLA class I antigen and NK cell activating ligand changes in malignant cells: current challenges and future directions. Adv. Cancer Res. 93, 189-234.
13. **Chang, C.-C.**, Campoli, M., Restifo, N.P., Wang, X., and Ferrone, S. (2005). Immune selection of hot-spot β_2-microglobulin gene mutations, HLA-A2 allospecificity loss and antigen processing machinery component downregulation in melanoma cells derived from recurrent metastases following immunotherapy. J. Immunol. 174, 1462-1471.
14. **Chang, C.-C.**, Campoli, M., Luo, W., Zhao, W., Zanker, K.S., and Ferrone, S. (2004). Immunotherapy of melanoma targeting human high molecular weight-melanoma associated antigen: potential role of non-immunological mechanisms. Ann. NY Acad. Sci. 1028, 340-350.
15. Campoli, M., **Chang, C.-C.**, Kageshita, T., Wang, X., McCarthy, J.B., and Ferrone, S. (2004). Human High Molecular Weight-Melanoma Associated Antigen (HMW-MAA): a melanoma cell surface chondroitin sulfate proteoglycan (MCSP) with biological and clinical significance. Crit. Rev. Immunol. 24, 267-296.
16. **Chang, C.-C.**, Campoli, M., and Ferrone, S. (2004). HLA class I antigen expression in malignant cells: why does it not always correlate with CTL-mediated lysis? Curr. Opin. Immunol. 16, 644-650.
17. **Chang, C.-C.**, Campoli, M., and Ferrone, S. (2003). HLA class I defects in malignant lesions: what have we learned? Keio J. Med. 52, 220-229.
18. **Chang, C.-C.**, Murphy, S.P., and Ferrone, S. (2003). Differential *in vivo* and *in vitro* HLA-G expression in melanoma cells: potential mechanisms. Hum. Immunol. 64, 1057-1063.

19. **Chang, C.-C.** and Ferrone, S. (2003). HLA-G in melanoma: can the current controversies be solved? Semin. Cancer Biol. 13, 361-369.

Book Chapters

1. Campoli, M., **Chang, C.-C.**, Oldford, S.A., Edgecombe, A.D., Drover, S., and Ferrone, S. (2004) HLA antigen changes in malignant tumors of mammary epithelial origin: molecular mechanisms and clinical implications. *In*: Breast Disease. Immunology of Breast Cancer, Wei, W.Z., Lopez, D.M. (eds), Amsterdam: IOS Press, 20: 105-125.
2. Pirozzi, G., **Chang, C.-C.**, Errico, S., Curci, A., Luongo, V., Paino, F., Di Gennaro, E., Ferrone, S., and Lombardi, M.L. (2004) Molecular defects underlying HLA class I antigen abnormalities in melanoma cells. *In*: HLA 2004: Immunobiology of the human MHC. Hansen J., Dupont, B. (eds.), Vol. I, pp. IHWG Press, Seattle, Washington.
3. Campoli, M., **Chang, C.-C.**, Wang, X., and Ferrone, S. (2003) HLA class I antigen processing machinery and HLA class I antigen derived peptide complex defects in tumor cell escape. *In*: Cancer Immunotherapy at the crossroad – How tumors evade immunity and what can be done, Finke, J.H., Bukowski, R.M. (eds). Totowa: The Humana Press Inc., pp. 3-34.

International Conference Proceedings

1. **Chang, C.-C.**, Luo, W., Wang, X., Ferrone, S., and Ghosh, D. (2006) Structural basis of tumor antigen mimicry by a mimotope isolated from a phage display peptide library. *J. Immunol.* 176: S261. The American Association of Immunologists 2006 Annual Meeting, Boston, MA.
2. **Chang, C.-C.** and Ferrone, S. (2004) HER2/neu-targeted breast cancer immunotherapy: a hybrid protein approach. The Susan G. Komen Breast Cancer Foundation 2004 Mission Conference, New York, NY.
3. Yamshchikov, G.V., Thompson, L., Mullins, D.W., Ferrone, S., Ogino, T., **Chang, C.-C.**, Galavotti, H., Aquila, W., Deacon, D., Ross, W., Patterson, J.W., Engelhard, V.H., and Slingluff, C.L., Jr. (2003) Immun escape, immune editing, and immune adaptation in a long-term survivor of metastatic melanoma. The 18th Annual Scientific Meeting of the International Society for Biological Therapy of Cancer, Bethesda, MD. *J. Immunother.* 26: S45, 2003
4. **Chang, C.-C.**, Pirozzi, G., Lombardi, M.L., and Ferrone, S. (2003) Identification of a *tapasin* gene mutation in a human melanoma cell line with HLA class I antigen downregulation. The 90th Annual Meeting of the American Association of Immunologists, Denver, CO. *FASEB J.* 17: C326, 2003.
5. Bandoh N., **Chang, C.-C.**, Cho, H.S., Wang, X, Ogino, T., Harabuchi, Y., Whiteside, T.L., and Ferrone, S. (2003) HLA class I antigen downregulation in human head and neck squamous cell carcinoma cell lines: Role of antigen processing machinery defects. The 94th Annual Meeting of the American Association for Cancer Research, Washington, D.C. *Proc. Am. Assoc. Cancer Res.* 44: 770, 2003.