ONICSCOUP <u>Conferences</u> <u>Accelerating Scientific Discovery</u> 2nd International Conference on **Translational & Personalized Medicine** August 05-07, 2013 Holiday Inn Chicago-North Shore, IL, USA

Class I MHC phosphopeptides are targets for immune system surveillance of cancer in humans

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Cells in the human body communicates their health status to the immune system by degrading cellular proteins and presenting fragments of each on the cell surface in association class I MHC proteins. Appropriately educated, cytotoxic T-lymphocytes (CTL) (CD8+ T-cells) bind to the class I MHC molecules on the cell surface, sample the protein fragments (peptides) being presented and kill those cells that express new peptides as a result of viral, bacterial and parasitic infection, tissue transplantation and cellular transformation (cancer). Since dysregulation of cell signaling pathways is one of the hallmarks of cancer, we hypothesized that class I MHC phosphopeptides that result from these pathways should be excellent candidates for use in the immunotherapy of cancer. We now find that Class I MHC phosphopeptides identified in preliminary work on leukemia, melanoma, colorectal, breast and ovarian cancers elicit pre-existing, central-memory, T-cell-recall responses in multiple, healthy blood donors. CD8 T-cell lines specific for these phosphopeptides recognize and kill both leukemia cell lines and HLA-matched primary leukemia cells *ex vivo*. Central memory recall responses to phosphopeptide antigens is absent in some leukemia patients and correlates with clinical outcome. The response is restored following allogenic stem cell transplantation. These results suggest strongly that class I MHC phosphopeptides are tumor targets of immune surveillance in humans and, therefore, are likely candidates for immunotherapy of cancer. Three of the discovered phosphopeptides will be the subject of a phase I clinical trial on melanoma later this year.

Biography

Donald F. Hunt joined the faculty at the University of Virginia as an Assistant Professor in September 1968 and currently holds the rank of University Professor with appointments in both Chemistry and Pathology. He is a co-inventor of more than 25 patents and patent applications and has more than 380 scholarly publications to his credit. His h-index of 84, (84 papers with 84 or more citations) ranks him among the top 130 living chemists in the world. Professor Hunt is the founder of PhosImmune Inc., a start-up cancer immunotherapy company.

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