Docket #: S05-346

Method for Imaging Cell Death in vivo

Programmed cell death (apoptosis) plays a crucial role in the pathogenesis of many diseases, such as AIDS and other viral illnesses, cerebral and myocardial ischemia, autoimmune and neurodegenerative states, organ and bone marrow transplant rejection, and tumor response to chemotherapy and radiation. Improved in vitro and histologic methods for the detection of apoptosis are rapidly expanding the understanding of the role of this process in the pathophysiology and are profoundly impacting drug development for a number of clinical disorders. An imaging technique capable of localizing and quantifying apoptosis in vivo would permit improved assessment of disease progression or regression, and similarly speed the development of therapy designed to inhibit or induce cell death.

One of the earliest events in apoptosis is externalization of phosphatidylserine (PS), a membrane phospholipid normally restricted to the inner leaflet of the lipid bilayer. Annexin V is an endogenous, low molecular weight, highly soluble human protein with a high affinity for membrane bound PS. The invention describes several radiolabeled forms of annexin V, which permit in-vivo assessment of the sites and degree of programmed cell death. As has been shown for annexin V reagents in vitro, annexin V radionuclide imaging permits a direct assessment of programmed cell death induced by transplant rejection, acute myocardial and cerebral infarction, tumor cell death induced by chemo or radiation therapy, and the macrophage cell death in experimental atherosclerosis. The in-vivo imaging method can be used serially in the same patient, to assess response to therapy over time.

This patented technology can be readily applied in the clinical setting to provide noninvasive assessment of disease progression or regression. This information can be used to determine the efficacy of therapies designed to inhibit or induce apoptosis.

Stage of Development
Radiolabeled annexin V imaging has been performed safely in human subjects, with no reported adverse events reported in studies of over 300 subjects.

Applications

- Non-invasive monitoring of organ or bone marrow transplant rejection
- Monitoring of cell death occurring with cerebral or myocardial ischemia
- Detection and monitoring of sites of infectious or noninfectious (autoimmune) inflammation prior to and during treatment
- Early assessment (24 hours) of tumor response to drug, radiation, or gene therapy
- In vivo imaging of cardiac allograft rejection
- Alzheimer's diagnosis

Advantages

- Safe and easily applied in clinical setting
- Useful in the diagnosis and monitoring of a variety of human disorders without the need for biopsy or when biopsy confirmation is not possible
- Portable, able to be used at bedside
- Uses existing clinical radionuclide imaging equipment

Publications

- Strauss, H. W., Blankenberg, F. G., Green, A. M., & Steinmetz, N. (2004). *U.S. Patent No. 6,726,895*. Washington, DC: U.S. Patent and Trademark Office.

Patents

- Published Application: 20030003047
- Published Application: 20040170603
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