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Targeting the elusive Sézary cell

The Sézary cell is a puzzling malignant vs activated white blood cell first discovered by dermatologist Albert Sézary. He L described the cell with a cerebriform nucleus in patients with erythroderma. Later it was found to be a T-cell by Lutz and others at the NIH and was suspiciously similar to HTLV-1 adult T-cell leukemia although no virus has yet been implicated. Recently, staging has been updated to include blood involvement for patients with SS and the mycosis fungoides form of cutaneous T cell lymphomas. The clinical features of SS are distinct from other forms of CTCL and include erythema >80%, keratoderma, ectropion, reactive adenopathy, and severe pruritus. The role of staphylococcus and drug induced disease suggests that some patients have persistent antigene stimulation as an initiating factor. Several other clinical Cutaneous T cell lymphomas (CTCL) have been described using clinical features, and histopathologic markers: The CD30 lymphoproliferative disorders, gamma delta lymphomas, subcutaneous panniculitic T cell lymphoma. The molecular basis for MF/SS has been the subject of intense basic research efforts. Genetic studies of the SS cell uncovered genetic instability with multiple deletions and gains seen by karyotyping and by array CGH. Whole genome sequencing of SS and MF DNA has revealed somatic mutations that may help us to understand what drives the proliferation of the SS cell. Understanding the pathogenesis of the SS cell has translated into new targeted therapies for both SS and MF. These include fusion proteins (denileukin diftitoxin and CD3-diptheria toxin), monoclonal antibodies targeted to CD4, CCR4, CD52, KIRD3L, and CD30. In addition, small molecules such as histonedeacetylase inhibitors have shown sensitivity in SS. Another break through has been in the area of non-ablative allogeneic stem cell transplant that offers cure to a subset of patients. In summary, the future looks bright to finally silence the elusive Sézary cell in the not too distant future.

Biography

Madeleine Duvic, MD, Professor of Internal Medicine and Dermatology, is Deputy Chairman of the Department of Dermatology at The University of Texas, MD Anderson Cancer Center in Houston, Texas. She received her medical degree from Duke University Medical School and completed an internship and residencies in internal medicine and dermatology, served as chief resident, and completed a fellowship in molecular biology and geriatrics. She is a former board member of the American Academy of Dermatology and recent Vice President of the Society for Investigative Dermatology. She was elected to the ADA and is a Founder and board member of the United States Consortium for Cutaneous Lymphomas. She serves on Medical and Scientific Boards of the National Alopecia Areata Foundation and Cutaneous Lymphoma Foundation and is the Principal Investigator of the Alopecia Areata Registry. She has authored over 420 peer-reviewed journal articles, two books, and has mentored numerous medical students, residents, fellows, and PhD students. She has been Principal Investigator of numerous clinical trials and translational research studies of T-cell mediated diseases and malignancies, including T-cell lymphomas, melanoma, and skin cancer. Her work is focused on developing and improving therapy for cutaneous T-cell lymphoma.

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