Folliculotropic Mycosis Fungoides

Panagiota Mantaka
Department of Dermatology, Oslo University Hospital, Oslo, Norway. E-mail: patty@aandahl.com

Panagiota Mantaka, dermatologist in Oslo, defended her thesis titled *Folliculotropic mycosis fungoides: A clinicopathologic, immunohistochemic and immunogenetic analysis* for the degree of PhD at the University of Oslo on November 14th, 2018. Main supervisor was Professor Jan Delabie, presently at the University of Toronto, Canada. Opponents were Professor Rudolf Stadler, University Medical Center Minden, Germany, Associate Professor Lars Helgeland, University of Bergen, and Professor Berit Flatø, University of Oslo. This thesis is available at https://www.duo.uio.no/handle/10852/65612.

Cutaneous T-cell lymphomas (CTCL) are a diverse group of lymphoproliferative diseases each of which is characterized by distinct clinical and histopathologic features. Mycosis fungoides (MF) is the most common CTCL. Within MF, subtypes of the disease are also recognized. Folliculotropic mycosis fungoides (FMF) is a subtype characterized by more pronounced involvement of skin appendages and importantly, has been reported to be associated with a worse prognosis than conventional MF. The pathogenesis of CTCL, including MF remains unclear. Even less is known about FMF.

Clinical and histopathologic findings of a Norwegian series of patients with FMF and of a control group with MF were described to explore the differences between FMF and MF (1). Further, T-cell receptor gene (*TR*) rearrangement analysis of skin biopsies of FMF patients obtained from different anatomic sites at time of diagnosis or during the course of disease was performed to investigate whether the disease arises from one or potentially multiple T-cell clones (2). Lastly, the amino acid sequence of the rearranged *TR* gene and the antigen-presenting cell subsets were studied in FMF and compared to that of MF to find potential evidence of selection by particular antigens (3).

These studies confirmed the distinct clinical and histopathologic features of FMF (1). Also, multiple T-cell clones were found in FMF during the course of the disease (2). This finding was an indication that chronic T-cell stimulation may be involved in the pathogenesis of FMF. Further *TR* sequence analysis showed a restricted *TRBJ* gene usage (*TRBJ2-1*, *TRBJ2-7*) with a recurrent EQ(Y/F)F amino acid motif (3). The EQ(Y/F)F motif is reported to be associated with T cells that are activated by lipid antigens through presentation by cluster of differentiation 1 molecules (CD1) on dendritic cells. A potential role for lipid antigen-stimulation in FMF was further corroborated by demonstrating an abundance of CD1c-expressing dendritic cells in FMF.

Future functional tests using tetramers will be required to ultimately prove lipid antigen-stimulation presented through CD1 lipids in FMF. The study of potential CD1-antigen restriction in FMF, and perhaps MF, is important in view of possible new therapeutic options, such as anti-CD1 antibodies.

Fig. 1. Panagiota Mantaka defended her thesis on November 14th, 2018. Foto: Foto- og videotjenesten, UiO.

List of original publications

1. Mantaka P, Helsing P, Gjersvik P, Bassarova A, Claussen OP, Delabie J. Clinical and histopathological features of folliculotropic mycosis fungoides: a Norwegian patient series. Acta Derm Venereol 2013; 93: 325–329.
2. Mantaka P, Malecka A, Trøen G, Helsing P, Gjersvik P, Delabie J. Multiple distinct T-cell clones in folliculotropic mycosis fungoides. Am J Dermatopathol 2014; 36: 972–976.
3. Mantaka P, Malecka A, Trøen G, Helsing P, Gjersvik P, Beiske K, Delabie J. Folliculotropic mycosis fungoides with skewed T-cell receptor CDR3 motif: suggestive of lipid antigen-selection? Acta Derm Venereol 2017; 97: 1081–1086.