Cutaneous T-cell lymphomas (CTCL) are extranodal non–Hodgkin’s lymphomas with clonal proliferation of skin-homing mature T-cells and pleomorphic skin lesions. Mycosis fungoides (MF), the most common and indolent form of CTCL, is characterized by epidermotropic effector memory T-cells, and Sézary syndrome (SS), an aggressive leukemic variant, is characterized by a triad of erythroderma, lymphadenopathy, and circulating clonal central memory T-cells. Few FDA-approved treatments for CTCL Patients with refractory or transformed MF/SS have a poor prognosis and therapy is usually palliative. Therefore, development of single agents and combination therapies with better therapeutic indices is critical.

I have been studying on CTCL for more than 25 years at the Beijing Medical University, the University of Zurich and the University of Texas MD Anderson Cancer Center since I was a postgraduate student in 1990. The following is our findings:

1. T-cell receptor gene rearrangements are helpful in making the diagnosis of early MF and for determining lymph node involvement.
2. Inactivation of tumor suppressor (p53) and activation of oncogenes (ras and myc) are associated with disease progression and tumor cell transformation in CTCL.
3. IL-7 and IL-15 protect CTCL cells against apoptosis by increasing the level of bcl-2 and bcl-x and STATs are constitutively activated in CTCL cells.
4. The equilibrium between apoptosis promoters and inhibitors is shifted to the side of the inhibitors during the progression of CTCL.
5. The absence of p15 and p16 proteins is due to the phosphorylation of RB protein rather than deletion or methylation of their genes in CTCL.
6. Bexarotene, an RXR-selective retinoid, at clinically relevant concentrations induces apoptosis of CTCL tumor cells, a therapeutic mechanism of bexarotene action in CTCL. Our findings supported approval of bexarotene by the FDA for treatment of patients with CTCL.
7. The PPAR-γ agonist CDDO selectively induces apoptosis of CTCL cells and bexarotene enhances CDDO-induced apoptosis. Our findings supported the development of a clinical trial of bexarotene in combination with rosiglitazone for the treatment of hematologic malignances including CTCL.
8. Histone deacetylase (HDAC) inhibitor vorinostat is effective for treatment of CTCL patients with an overall response rate of 24%. HR23B is a
potential biomarker for tumor sensitivity to HDAC inhibitor-based therapy in CTCL.

9. Curcumin can down-regulate protein expression of STAT3/p-STAT3 as well as STAT3-regulated genes, and suppresses the DNA binding of NF-κB in CTCL cells, indicating the potential therapeutic option for patients with CTCL.

10. Matrine (an alkaloid found in plants of the Sophora family) alone and combined with IFN-α at clinically relevant concentrations can induce apoptosis in CTCL cells, providing the laboratory rationale for treatment of CTCL patients.

References