

MERKEL CELL CARCINOMA IN ISRAEL: BEILINSON'S EXPERIENCE

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TO THE EDITOR:

We read with great interest the article by Toledano and colleagues [1] about Merkel cell carcinoma (MCC). The authors described demographic and tumor characteristics of 17 patients seen at Shaare Zedek Medical Center between 2015 and 2022.

The authors claimed that “data on MCC, especially from tertiary centers in Israel, is limited,” without providing a reference to document their statement. We would like to argue the opposite.

The Institute of Oncology (Davidoff Cancer Center) at Rabin Medical Center has been a referral center for patients with MCC for many

years. Even though MCC is indeed a rare disease, our database now includes 271 patients.

We have described, in at least 21 publications, both basic research and clinical features on MCC, including clinical presentation and treatment modalities such as radiotherapy and chemotherapy. Our research emphasizes the role of adjuvant radiation therapy after the excision of the primary tumor and the chemosensitivity of widespread disease, and more recently, immunotherapy with avelumab. We have discussed the frequent occurrence of second malignancies in these patients, a description of infrequent primary sites such as the eyelid [2], and recently, the gluteal region [3]. Our series on the latter is the largest published to date (25 patients). We have described the expression of cyclooxygenase-2 and of c-kit protein in both primary and metastatic MCC.

Demographic data on 251 patients, which we published [4], showed that the median age of these patients was 74 years and 41% were female, while Toledano et al. [1] reported a mean age of 70 years (mey-

ears; 59% female. The most frequent primary sites in our patients are, as expected, sun-exposed areas such as upper and lower limbs and face.

In summary, our group has accumulated vast experience in MCC and our series is certainly the largest in Israel. Data in Israel on MCC is not “limited”.

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Capsule

A combinatorial transcription factor screening platform for immune cell reprogramming

Direct reprogramming of immune cells holds promise for immunotherapy but is constrained by limited knowledge of transcription factor (TF) networks. Kurochkin and colleagues developed REPROcode, a combinatorial single-cell screening platform to identify TF combinations for immune cell reprogramming. First, the authors validated REPROcode by inducing type-1 conventional dendritic cells (cDC1s) with multiplexed sets of 9, 22, and 42 factors. With cDC1-enriched TFs, REPROcode enabled identification of optimal TF stoichiometry, fidelity enhancers, and regulators of cDC1 states. Then they constructed an arrayed

lentiviral library of 408 barcoded immune TFs to explore broader reprogramming capacity. Screening 48 TFs enriched in dendritic cell subsets yielded myeloid and lymphoid phenotypes and enabled the construction of a TF hierarchy map to guide immune reprogramming. Finally, they validated REPROcode's discovery power by inducing natural killer (NK)-like cells. This study deepens our understanding of immune transcriptional control and provides a versatile toolbox for engineering immune cells to advance immunotherapy.

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