

THE STATE OF ISRAEL
MINISTRY OF HEALTH
THE CHAIM SHEBA MEDICAL CENTER
Affiliated to the Tel-Aviv University
Sackler School of Medicine
TEL-HASHOMER 52621, ISRAEL



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המרכז הרפואי המשולב ע"ש חיים שיבא
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August 1st, 2019

Dear ICA USA Board of Directors

At the end of the second funding year, I would like to thank you for your support of my research project, titled: "Turning response to neoadjuvant therapy into a predictive biomarker for personalized treatment in high grade serous ovarian cancer", for the years 2017-8.

Unlike major strides in the treatment of other malignancies, the realm of ovarian cancer patients remains frustrating: All patients will receive a chemotherapy protocol that was hardly updated in the past 3 decades, despite the fact that the benefit to the patient is expected to be low, and the recurrence rates are extremely high. Often patients receive 3 cycles of chemotherapy before undergoing surgery, and continue with the same protocol although its effectivity was minor. We hypothesized that the response to pre-surgical (neoadjuvant) chemotherapy can be used as a biomarker to guide post-surgical therapeutic decisions. In this project we focused on one genomic aberration, amplification of the gene *CCNE1*, which was previously implicated with lack of response to chemotherapy. We tested whether this defect can be reliably determined on biopsies taken from ovarian cancer patients before initiation of therapy, and whether it correlated with lack of response. Surprisingly for us, we discovered the *CCNE1* expression did not correlate with clinical benefit from chemotherapy. Furthermore, the residual tumors after chemotherapy were not enriched for *CCNE1*. We wished to use *CCNE1* staining as a biomarker to guide biologically targeted treatment of ovarian cancer, which did not respond adequately to pre-surgical chemotherapy; however the negative results in the first part of this research did not support progression in this direction. Nonetheless, our concept attracted enough interest to be published in the journal *Oncotarget* (<http://www.oncotarget.com/index.php?journal=oncotarget&page=article&op=view&path%5B%5D=19272>). We now plan to continue this approach and more broadly look for biomarkers in order to define subsets of patients for whom targeted drugs may have greater clinical value than the current standard chemotherapy protocols.

The continuous support of ICA to translational research performed by clinicians in Israel is one of the cornerstones of my own and my colleagues' activity. I would like, once again, to thank you for your support.

Sincerely,

A handwritten signature in black ink that reads "Levanon Keren". The signature is written in a cursive style with a light blue shadow effect behind the text.

Keren Levanon, MD, PhD
Sheba Cancer Research Center
Chaim Sheba Medical Center
Ramat Gan, Israel