

Welcome to the second edition of the CRS FG NND Newsletter!!

It is our pleasure to bring you the latest edition of the CRS Nanomedicine and Nanoscale Delivery Focus Group (CRS NND FG) newsletter. We hope this second edition will keep you updated on our latest news and recent activities, while sharing with you some of the most outstanding achievements of our members. Enjoy!

Celebrating the achievements of our CRS NNDD Focus Group members



Ronit Satchi-Fainaro, Ph.D., is a Professor of Pharmacology in the Department of Physiology and Pharmacology at the Sackler Faculty of Medicine, Tel Aviv University. She leads a multidisciplinary group of 30 scientists that pursues translational research encompassing the discovery of new molecular targets that guide the design and synthesis of advanced polymer-based nanosystems, for the treatment of cancer based on interruption of tumor-host interactions.

She previously served as President of The Israeli Controlled Release Society (CRS) (2010-2015). We were very happy to learn that she was recently awarded three research grants of excellence, which we celebrate by sharing with you her history and understanding how her passion about nanomedicine and biomedical nanotechnology boosts her research.

Q. Can you tell us about yourself and your background?

A. I received my B. Pharm. from the Hebrew University in Jerusalem in 1995 and my Ph.D. in Polymer Chemistry and Cancer Nanomedicine from the University of London in 1999 with Prof. Ruth Duncan. Then, I spent four years as Postdoctoral Research Fellow at Harvard University and Children's Hospital Boston working with Prof. Judah Folkman on Vascular and Cancer Biology. In 2003, I was appointed Instructor in Surgery at Boston Children's Hospital and Harvard Medical School, and in 2006 I joined Tel Aviv University.

Q. Why did you become a scientist? What were the major findings that have led up to your interest in your current area of research?

A. During my military service at Sheba hospital, I witnessed the devastating impact that the chemotherapy-induced side-effects had on cancer patients. After graduating my Pharmaceutical Sciences degree at the Hebrew University's Faculty of Medicine, and my internship in the pharma industry, I decided to look for a direct Ph.D. track that would allow me to find new effective and selective drugs against

This publication reflects only the views of the Focus Group NND board. We welcome contributions from members of our focus group community.

cancer. My decision to pursue my Ph.D. research studies in polymer chemistry and cancer research with Professor Ruth Duncan at the London School of Pharmacy was really fast! I imagined those polymers developed to deliver drugs to cancer cells, as the robots entering the bloodstream and coming exactly where they should go. At the end of my Ph.D., I met Professor Judah Folkman at the Polymer Therapeutics Symposium in London. I was fortunate to speak right after his plenary lecture where, unlike his routine, Folkman stayed for the whole session. He suggested that in addition to the development of cancer cells-targeted drugs, we should treat the cancer-supporting tumor microenvironment to block tumor mass growth and metastasis. Folkman was the first to describe that tumor cells are angiogenesis dependent. During my postdoctoral fellowship in his lab, we combined the field of polymeric nanomedicine and anti-angiogenic drugs to starve the tumor in a selective manner.

Q. What can you tell us about your ongoing projects? What is your favorite aspect of your research?

A. My multidisciplinary research laboratory focuses on basic research elucidating the mechanisms underlying the switch from cancer dormancy leading to the discovery of new molecular targets interrupting tumor-host interactions. This is indeed an exciting approach that aims to design highly selective targeting molecules integrating biology, chemistry, medicine, bioinformatics and nanotechnology to selectively guide drugs into pathological sites

Q. Can you share with us a turning point in your work as a scientist?

A. I see great importance in the field of our research taking researchers from different disciplines. It took me quite a while to integrate what I did in my doctoral thesis with a focus on the chemistry and synthesis of polymeric nanoparticles, along with the biological and medical part I worked on at my postdoc at Harvard, which means recruiting people from different disciplines who speak entirely different languages.

I believe that this led to a unique research approach. It starts at the operating room of the surgeons with whom we collaborate. We receive tissue samples from patients and once the biologists screened, discovered and validated new molecular targets overexpressed in a certain cancer type, the chemists synthesize the nano-based targeted systems, which are then tested back by the biologists on the disease models established and validated in the lab. This includes animal models, but also three-dimensional (3D)-printed cancer models. Together with the engineers in the lab, we developed 3D-spheroid systems composed of cancer cells and all the stromal cells including those of the immune system, connective tissue, blood vessels, etc., depending on the organ from which the tumor arose. This is really exciting as we print mini-tumors that look like the original tumor the patient had with his individually tailored cells. We can print ten of these tumors and test them for their sensitivity to different therapies including the nanomedicines we design.

Q. Recently, you were awarded the highly competitive ERC Advanced, ERC Proof of Concept and MRA Established Researcher awards!! Congratulations! These are exceptional achievements granted to bright minds by giving them the opportunity to pursue their pioneering work. In your opinion, to what extent the Nanomedicine and Nanoscale Delivery field was relevant for those projects clearly recognized by the international scientific community worldwide as being able to change people's lives?

A. Cancer is still the deadliest disease worldwide! And the development of new therapies selectively active against cancer cells in the right amount and during the necessary period without inducing resistance continues to be an urgent medical unmet need! The common denominator between all the different projects we run in my lab, is the discovery and understanding of the interactions between the cancer cells and the microenvironment cells, which guide the development of nanotechnology-based tools to neutralize this disturbance so that the tumor cannot progress and will be destroyed. While being highly multidisciplinary approaches, in all these projects I maintain an interest in understanding the biological rationale for the design of nanomedicines suitable for clinical translation. Nanotechnology is indeed a crucial element in this continuous search for answers to these devastating diseases, against which we do

not have solutions, such as melanoma, lung and breast brain metastases and glioblastoma, which are at the focus of these grants that I was recently awarded.

Q. In your opinion, what are some of the biggest challenges in the Nanomedicine and Nanoscale Delivery field?

A. We do know that a nanomedicine is complex! It is much more complex than small drugs, for example. However, it is our job to demonstrate that we know how to control their synthesis and fully characterize their physico-chemical properties at a reasonable cost and a rapid, reproducible and robust manner. Moreover, it is paramount that we will be able to predict how these systems will behave under physiological and pathological conditions. Their complexity is also what makes them so special, interesting and promising. They offer potential solutions against diseases for which other simpler options were not sufficient! The advanced knowledge on the disease-related mechanisms, at cellular but also molecular levels, shows that these devastating diseases can only be defeated by combinational approaches. This is clear from the clinical settings, in which we exploit diverse combinations of multiple drugs. Here, we can anticipate a great contribution of the nanoscale delivery field. We live in an amazing era of technological advances- things we couldn't imagine doing (if at all) 20 years ago, like high-throughput screening, single cell RNAseq, microbiome analysis and antibodies engineering, became an affordable routine! Just look at the fascinating agenda of the GRC on Cancer nanotechnology which I'm chairing next week or the upcoming CRS in Valencia- it makes me really optimistic about the future!

Nanocarriers targeted delivery for female cancers
by Prof. Balu Ranganathan, Palms Connect LLC, USA

Globally 7 women die per minute of cancer, of which two die of female cancers per minute, leading to 1.1 million deaths (GLOBOCAN, 2018) per year, resulting in psychological, financial and societal (breakup / divorce) ruin of the families. It contributes to the enormous economic and social burden for the federal governments hindering the upliftment of the quality life of the citizen population. In 2018, 626,679 women died of breast cancer, 311,365 women died of cervical cancer and 184,799 women died of ovarian cancer. Indeed, cumulatively 1.1 million women died of female cancer in 2018, 85,779 of which in the age group of 20-39.

A biologically active drug administered as a nanoscale delivery system constitutes one of the most promising tools for female cancer eradication. More than a decade ago, the nanomedicines Doxil[®] (2003) and Abraxane[®] (2005) were approved by the FDA for breast cancer treatment.

The clinical success of nanomedicine relies on the prolonged and controlled delivery of the drug payload to the targeted tumor site, thus avoiding off-target effects, and thereby rendering the drug regimen to have a very high efficacy over a period to nullify recurrence. This is very critical for the particularly aggressive basal-like breast cancer subtype, which has high incidence of recurrence. The development of drug resistance constitutes another bottleneck of conventional chemotherapeutic formulations, which can also be circumvented by nanoformulations since the right dosage reaches (enhanced permeability and retention {EPR} effect) the susceptible cells leading to the suppression of tumor growth, apoptosis and finally tumor shrinkage.

Cancer cannot be cured in a day! The **Controlled Release Society**, founded in 1978, is a leading society with members from diversified technology development areas focusing on delivery science and technology. It is now one of the pioneer societies and the areas of research of **the CRS Nanomedicine and Nanoscale Delivery Focus Group** include the development of nanodrug delivery systems against female cancers. These advanced female cancer therapies and thereby the cure of these patients, do require the integration of biomolecular engineering (chemical engineering & biotechnology) with big data analytics, artificial intelligence and additive manufacturing.

The academic research, clinical and industrial convergence among FG NND members may pave way for revolutionary nanomedicines, which will minimize toxic side-effects, as well as improve the therapeutic index of anti-cancer drugs, patients' well-being post diagnosis and finally lead to disease-free survival of the individual women.

CRS NND FG News and Social Media Corner

Our CRS NND FG Focus Group has been highly active on Twitter (https://twitter.com/CRS_FG_NANO) and LinkedIn (<https://www.linkedin.com/groups/12138578/>)!!

Our first webinar with **Dr. Jeffrey D. Clogston** (Nanotechnology Characterization Laboratory) on the topic of "**Nanomedicine Development: Lessons Learned, Approval Earned**", and moderated by **Prof. Ruth Schmid** (FG board member and past-president at CRS) was a success! Take a look at the webinar video following the link <https://youtu.be/ApGa0COjZz4>.

Join us at the CRS Annual Meeting & Exposition!!

Several CRS NND FG members will be highly active! Take a look at the program <https://2019.controlledreleasesociety.org/program>



Focus Group Membership Meeting
Monday, July 22, 2019
7:00 AM to 8:00 AM

Focus Group Scientific Session
Wednesday, July 24, 2019
10:00 AM to 12:00 AM

CRS NND FG AWARDS will be announced during our scientific session!!

Translational Research (NEW!!)

Fundamental Research (NEW!!)

Young Investigator Award

Trainee Award