Bar-Ilan University
אוניברסיטת בר-אילן

Faculty of Exact Sciences
Department of Chemistry

הפקולטה למדעים מדויקים
המחלקה לכימיה

S E M I N A R

Monday 31/12/18, 12:00 pm

Building 211, seminar room

SPEAKER:

Dr. Ofer Shamni

Cyclotron unit, Hadassah Hospital, Ein-Karem, Jerusalem

TOPIC:

"Research and Development" challenges in PET radiopharmaceuticals field for comprehensive molecular imaging

In 1997, the first and only university/hospital-based cyclotron in Israel was installed at the Hadassah-Hebrew University Hospital. Preclinical investigations of radiolabeled and cold compounds are carried out *in vitro*, *ex vivo* and *in vivo*, using dedicated laboratories equipped with a microPET/ CT scanner. Collaboration with the Nuclear Medicine department at Hadassah, allow the access to a clinical PET/ CT scanner, and preclinical studies of larger animals, such as non-human primates. The unit produces, on a daily basis, several PET imaging agents for clinical use and clinical studies such as [^{18}F]FDG, [^{18}F]FDOPA, [^{18}F]FLT, [^{18}F]PSMA and [^{18}F]Flutemetamol. Throughout the years, our unit developed several novel PET radiopharmaceuticals, employed in the fields of oncology and cardiology.
Three projects are described herein:

The fluoroethylerlotinib (FEE) project focuses on the development of novel ^{18}F-labeled erlotinib analogs for non-invasive identification of non-small cell lung cancer (NSCLC) tumors that harbor activating mutations in the EGFR gene, using PET molecular imaging. This approach should enable non-invasive identification and selection of patients prior to tyrosine kinase inhibitors (TKI)-targeted therapy. The ability of [^{11}C]erlotinib PET to non-invasively identify tumors that harbor activating mutations in the EGFR gene has been demonstrated in several clinical trials and pre-

clinical studies. In order to overcome the challenges related to the short half-life of ^{11}C, we introduced and patented a new ^{18}F-labeled erlotinib derivative. The anti-proliferative activity of FEE was investigated and confirmed *in vitro*, using human NSCLC cell cultures possessing the different mutations in the tyrosine kinase receptor. Furthermore, *in vivo* PET/CT imaging studies of NSCLC tumor-bearing mice following i.v injection of [^{18}F]FEE demonstrated its potential as a molecular imaging probe for identifying EGFR with activating mutations.

The goal of the ammonium salts project is to develop a PET probe for imaging myocardial perfusion. The carbon-11-labeled lead compound, [^{11}C]DMDPA, was evaluated in phase-I clinical trials with 12 healthy volunteers. Based on its chemical structure and the collective biological data obtained, we designed a family of new ammonium compounds labeled with ^{18}F. This technology was licensed to radio-pharma company, and [^{11}C]DMDPA is currently undergoing phase-II clinical trials.

The third project involves the development of a novel F-18 labeled compound ([^{18}F]fluoroethylquinolinium, [^{18}F]FEtQ) for identifying metastatic colorectal cancer (mCRC) patients who will respond to oxaliplatin-based chemotherapy. CRC is the third most common cancer in men and the second in women worldwide, and approximately 20% of patients with CRC already have metastases at diagnosis. For metastatic and/or recurring CRC oxaliplatin based-chemotherapy (FOLFOX) is available, with reported response rates of about 60% after first-line treatment. Consequently, ~40% of CRC patients are unnecessarily subjected to the harsh oxaliplatin-based treatment regimen. At present, there is an unmet clinical need for non-invasive methodologies that can provide systemic information on tumor responsiveness prior to treatment with oxaliplatin-based chemotherapy. We hypothesized that the responsiveness for oxaliplatin-based chemotherapy is mediated by the organic transport cation transporter (OCT). We demonstrated OCT involvement in the cellular uptake of oxaliplatin. In this project we aim to determine if the novel PET tracer, [^{18}F]FEtQ, structurally derived from a known OCT inhibitor, can be employed as a non-invasive screening modality for molecular imaging of the OCT and for predicting treatment outcome of mCRC patients with oxaliplatin-based chemotherapy.