BIOGRAPHICAL SKETCH

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NAME: Galun Eithan

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POSITION TITLE: Professor of Gene Therapy, Director Goldyne Savad Institute of Gene Therapy

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Tel Aviv University	M.D.	1972-1979	Medicine
Hebrew University	Board	1983-1986	Internal Medicine
Hebrew University	-	1986-1989	Hepatology
Harvard Medical School	-	1989-1991	Fellowship Hepatology

A. Personal Statement

Who Am I: I am a full professor of Gene & Cell Therapy at the Hebrew University of Jerusalem. Over the last 20 years, I have directed the Gene and Cell Therapy Institute at the Hadassah Hebrew University Hospital that I have established. This entailed the collection of funding for the building of the institute during the seed stage and recruiting and funding all of the research activities from grant money, collaborations with the industry and fundraising. Today, we are 10 research groups, with 70 investigators. In addition to the research groups, I have established a GMP level production facility with four clear rooms engaged in the production of biological materials (including viral vectors, devices, therapeutic cells, e.g., mesenchymal stem cells and human embryonic stem cells) administered to humans in phase I/II studies.

Major achievements in the recent academic career: My achievements are concentrated in the field of translational medicine and include: **1.** Development of hepatitis B and C viruses monoclonal antibodies that progressed into phase II clinical studies, and the development of the Trimera HBV and HCV mouse models to assess the anti-viral effects of these antibodies. **2.** Understanding the molecular and cellular factors that play a role in the biological axis of liver inflammation → regeneration → cancer (hepatocellular cancer). **3.** Development of novel gene therapy platforms, e.g., the usage of ultrafast infrared femtosecond laser for dermal, muscle and retinal naked DNA transfection.

Current research interest relevant to this program: Our group investigated the role of inflammatory factors contributing to liver regeneration upon infection. While investigating these factors along the years, we have learned that the IL6-gp130 pathway is pivotal for the regeneration of liver parenchyma. This understanding further engaged us in studies aimed at translating the knowledge generated to determine the role of IL6-gp130 in the regeneration and anti-apoptosis in other tissues. Our current data show that this pathway is involved in the protection and regeneration of the kidney, heart, bone marrow stem cells and the salivary gland. In the recent years we have also been investigating the significance of microRNAs in the regulation of physiological and pathological human conditions by studying mouse models. These have revealed some astonishing results. One is the role of miR 122 in controlling lipid metabolism, influencing anemia development and encountering anti-tumor properties.

Translational research: Our researchers at the institute and I, in particular, are believers in translational investigation. During recent years, I have been involved in a number of programs and these include: 1. Development of a novel therapy for pancreatic cancer based on siRNA targeting K-Ras (I established a company around this technology called Silenseed); 2. Development of FIV as a novel lentiviral vector for gene therapy. 3. Identification of new therapeutic targets for liver cancer. 4. Development of novel imaging technologies for the identification of liver pathology, tools that were further used in our program on liver inflammation → regeneration → cancer (hepatocellular cancer).

Director of the Hadassah biologicals production site (the good manufacturing production (GMP)): I had established in 1997 the Hadassah GMP facility for biologicals. Since its creation we have produced 50 different 1st in man products. These were either our products of the gene therapy institute, or from the hospital or collaborations with out-side investigators and companies. This year, we have reached an unprecedented achievement: We are the only worldwide academic facility which received a phase 3 license from the government ministry of health to produce a therapy. This product is also approved by the FDA for a phase 3

B. Positions and Honors

Internships and Residencies:

1978-1979 Internship, Hadassah University Hospital
1983-1988 Residency, Department of Internal Medicine A, Hadassah University Hospital, Jerusalem
1988-1989 Chief Resident, Internal Medicine, Hadassah University Hospital, Jerusalem

Research Fellowships:

1981-1983 Heller Institute of Physiology, Tel Hashomer Hospital
1986-1987 Research Fellow, Weizmann Institute of Science, Rehovot
1989-1991 Molecular Hepatology Laboratory and MGH Cancer Center, Harvard Medical School

Academic Appointments:

1985-1988 Instructor in Medicine, The Hebrew University, Jerusalem
1988-1991 Lecturer in Medicine, The Hebrew University, Jerusalem
1991-1999 Senior-Lecturer in Medicine, The Hebrew University, Jerusalem
1998- Director, Goldyne Savad Gene Therapy Institute Hadassah University Hospital
2000-2004 Associate Professor of Medicine, Hebrew University, Jerusalem
2005- Full Professor of Gene Therapy, Hebrew University, Jerusalem
2009 - Visiting Professor University of Eppendorf Hamburg
2020 - Member of The Israeli National Academy for Science in Medicine

Awards:

1987 Outstanding Lecturer in Internal Medicine, The Hebrew University, Jerusalem
1989 Rothschild Fellowship Award
1990 Henry Leon Weiler Fellowship Award
1992 Naftali Foundation Award
2000 Chair, Sam and Ellie Fishman Cathedra in Gene Therapy
2008 Elkales Medicine Prize
2010 Raskin – Exiqon (USA/Denmark)
2011 Wolfson Family (UK), twice also at 2013
2013 Wohl Foundation (UK)
2014 Selma Kron Trust A (USA)
2015 Robert Benson Trust (USA)
2016 Washington University, St Louis Award (USA)
2018 Recipient of an ERC Advance

C. Contribution to Science

Basically, I'm a physician who believes in translational science. In addition to the numerous research fields along the years in which I have directly contributed, as can be depicted from the below relevant specific investigative fields, I am confident that I have also made a major contribution to students science education. I had invested significantly during more then 30 years in teaching medical school students, undergraduates and graduate, and through these educational sessions influenced them to take part in the translational medicine world. Many of these had then engaged in MD/PhD programs. I had been teaching many residence physicians and many of them came to conduct PhDs after they completed their MD or residency learning. At each time point of my academic life I had personally at least 7 PhD/MSc students. Accordingly, I view my educational investment in students and also peers as a major contribution to science.

As a hepatologist. most of my studies are a result of questions initiated in the clinic, directly or indirectly. To the current date, my articles have over 9000 citations. Below are some of the specific scientific areas in which I had conducted my research and to which I had contributed:

Gene Therapy: Although it may seem simple and straightforward, gene therapy is a very challenging field of translational medicine. One major difficulty is the implementation of efficient/effective delivery systems. The cited work below highlights key programs that I have been involved in - most of these aimed at overcoming delivery obstacles. Our most recent delivery platform had completed a phase 1 clinical investigation and is now had already initiated a phase 2 study in two sites in the USA after an FDA approval (the phase 1 was performed in Israel). In this study we show that a biodegradable scaffold is able to shed from within a tumor siRNA targeting K-RAS^{mut} and encounter a significant anti tumor effect. The pre-clinical results of this study are published in PNAS as depicted below:

Lippin Y, Dranitzki-Elhalel M, Brill-Almon E, Mei – Zahav C, Mizrachi S, Liberman Y, Iaina A, Kaplan E, Podjarny E, Shani N, **Galun E**. (2005). Human erythropoietin gene therapy for patients with chronic renal failure. Blood 106:2280-2286.
Freeman AI, Zakay-Rones Z, Gomori JM, Linetsky E, Panet A, Libson E, Linda R, Greenbaum G, Irving CS, **Galun E**, Siegal T. (2006). PhaseI/II trail of intravenous NDV-HUJ (OV001) oncolytic virus in recurrent glioblastoma multiforme. Molecular Therapy 13:221-228.
Zeira E, Manevitch A, Manevitch Z, Kedar E, Gropp M, Daudi N, Barsuk R, Harati M, Yotvat H, Troilo P, Griffiths T, Pacchione S, Roden D, Niu Z, Nussbaum O, Zamir G, Pappo O, Hemo I, Lewis A, **Galun E**. (2007). Femtosecond laser - A new intradermal DNA delivery method for efficient, long-term gene expression and genetic immunization. FASEB J 21:3522-33.
Zorde Khvalevsky E,Gabai R,Rachmut I-H, Horwitz E, Brunschwig Z, Orbach A, Shemi A, Golan T, Domb A, Yavin E, Giladi H, Rivkin L, Simerzin A, Elyakim R, Kalila A, Hubert A, Lahav M, Kopelman Y, Goldin E, Dancour A, Hants Y, Arbel-Alon S, Abramovitch R, Shemi A, **Galun E**. (2013). Mutant KRAS as a druggable target for pancreatic cancer. Proc Natl Acad Sci (USA) 110:20723-8.
Golan T, Zorde Khvalevsky E, Hubert A, Malka Gabai R, Hen N, Segal A, Domb A, Harari G, Ben David E, Raskin S, Goldes Y, Goldin E, Eliakim R, Lahav M, Kopleman Y, Dancour, Shemi A, **Galun E**. (2015). RNAi therapy targeting KRAS in combination with chemotherapy for locally advanced pancreatic cancer patients. Oncotarget 6:24560-70.
Abraham M, Pereg Y, Bulvik B, Klein S, Mishalian I, Wald H, Eizenberg O, Beider K, Nagler A, Golan R, Vainstein A, Aharon A, **Galun E**, Caraco Y, Or R, Peled A. (2017). Single Dose of the CXCR4 Antagonist BL-8040 Induces Rapid Mobilization for the Collection of Human CD34+ Cells in Healthy Volunteers. Clin Cancer Res. 23:6790-6801.
Nagler A, Shimoni A, Avivi I, Rowe JM, Beider K, Wald H, Tiomkin L, Ribakovsk L, Riback Y, Ramati Y, Aviel S, **Galun E**, Shaw HL, Eizenberg O, Abraham M, A Peled. (2019). Phase I/II Stem Cell Mobilization Study with the High Affinity CXCR4 Antagonist BKT140. Clin Cancer Res (in press).

Hepatitis B virus (HBV) and Hepatitis C virus (HCV): Until quite recently, I have been engaged in the attempt to develop novel approaches for the treatment of HBV and HCV. Two decades ago, it was obvious that the most essential barrier for the development of efficient anti hepatitis drugs, in addition to the basic understanding of HBV and HCV biology, was the fact that there was no animal model to assess the drugs. In addition, the recurrence of both HBV and HCV infection in transplanted liver in patients who are carriers of either virus was a major challenge. Accordingly, we developed the first HBV and HCV small animal models – the Trimera mice with HBV and HCV. In these models we could investigate the properties of anti-hepatitis drugs for the relevant clinical indications. We could assess anti-HBV and anti-HCV human monoclonal antibodies that we have developed and also tested these later in humans in clinical studies. The most prominent reports on the animal models, the effect of the anti-hepatitis monoclonal antibodies in the animal models and the clinical development are depicted below):

Ilan E, Burakova T, Dagan S, Nussbaum O, Lubon I, Eren R, Ben-Moshe O, Arazi J, Berr S, Neville L, Yuen L, Mansour TS, Gillard J, Eid A, Jurim O, Shouval D, Reisner Y, **Galun E**. (1999). The HBV - Trimera mouse: A model for human HBV infection and evaluation of anti-HBV therapeutic agents. Hepatology 29:553-62.

Ilan E, Arazi J, Nussbaum O, Zauberman A, Eren R, Lubin I, Ben-Moshe O, Kischitzky A, Litchi A, Margalit I, Gopher J, Mounir S, Cai W, Daudi N, Eid A, Jurim O, Czerniak A, **Galun E**, Dagan S. (2002). The hepatitis C virus - Trimera mouse: A model for evaluation of anti-HCV therapeutic agents. J Infectious Disease 185:153-61.
Galun E, Eren R, Safadi R, Ashour Y, Terrault N, Keeffe EB, Matot I, Mizrachi S, Terkieltaub D, Zohar M, Lubin I, Gopher J, Shouval D, Dagan S. (2002). Clinical evaluation (phase I) of a combination of two human monoclonal antibodies to HBV: safety and antiviral properties. Hepatology 35:673-679.
Eren R, Landstein D, Terkieltaub D, Nussbaum O, Zauberman A, Ben-Porath J, Gopher J, Buchnick R, Kovjazin R, Rosenthal-Galili Z, Aviel S, Ilan E, Shoshany Y, Neville L, Waisman T, Ben-Moshe O, Kischitsky A, Foung SKH, Keck Z-Y, Pappo O, Eid A, Jurim O, Zamir G, **Galun E**, Dagan S. (2006). Preclinical evaluation of two neutralizing human monoclonal antibodies against HCV: A potential treatment to prevent re-infection in liver transplant patients. J Virology 80:2654-2664.
Galun E, Terrault N, Eren R, Zauberman A, Nussbaum O, Terkieltaub D, Zohar M, Buchnik R, Ackerman Z, Safadi R, Ashur Y, Misrachi S, Liberman Y, Rivkin L, Dagan S. (2007). Clinical Evaluation (Phase I) of a Human Monoclonal Antibody against Hepatitis C Virus: Safety and Antiviral Activity. J Hepatology 46:37-44.
Gozlan Y, Bucris E, Shirazi R, Rakovsky A, Ben-Ari Z, Davidov Y, Veizman E, Saadi T, Braun M, Cohen-Naftaly M, Shlomai A, Shibolet O, Zigmond E, Katchman H, Menachem Y, Safadi R, **Galun E**, Zuckerman E, Nimer A, Hazzan R, Maor Y, Saif AM, Etzion O, Lurie Y, Mendelson E, Mor O. (2019). High frequency of multiclass HCV resistance-associated mutations in patients failing direct-acting antivirals: real-life data.
Antivir Ther. 24:221-228.

Liver inflammation: The liver is a very unique organ in a sense that upon chronic inflammation the liver responds in regeneration to overcome the tissue loss. However, numerous pathological conditions develop which contribute later to the development of hepatocellular carcinoma (HCC). Prior to the investigation, and later on in parallel to the studies aimed to understand the mechanism of how inflammation in the liver causes HCC, we were interested to identify mediator of regeneration in the inflamed liver, and to better understand the contribution of these factors both to the inflammatory process as well as to the regenerative process. We are currently investigating this, and in a report in preparation we show that microRNA 675, which is derived from the lncRNA H19, targets FADD and by this shifts the inflammatory signal of TNFα coming from macrophages to necroptosis.
Lavon I, Goldberg I, Amit S, Jung S, Tsuberi BZ, Barshak I, Kopolovic J, **Galun E**, Bujard H, Ben-Neriah Y. (2000). High susceptibility to bacterial infection, but no liver dysfunction, in mice compromised for hepatocyte NF-kappaB activation. Nature Medicine, 6:573-7.
Khvalevsky E, Rivkin L, Rachmilewitz J, **Galun E**, Giladi H. (2007) TLR3 signaling in a hepatoma cell line is skewed towards apoptosis. Journal of Cellular Biochemistry 100:1301-12.
Ben Moshe T, Barash H, Kang TB, Kim JC, Kovalenko A, Gross E, Schuchmann M, Abramovitch R, **Galun E**, Wallach D. (2007). Role of caspase-8 in hepatocyte response to infection and injury in mice. Hepatology. 45:1014-24.
Zorde-Khvalevsky E, Abramovitch R, Harel-Barash H, Rivkin L, Spivak-Pohis I, Rachmilewitz J, **Galun E**, Giladi H. (2009). TLR3 signaling attenuates liver regeneration. Hepatology 50:198-206.
Rivkin M, Zorde-Khvalevsky E, Simerzin A, Chai C, Yuval JB, Rosenberg N, Harari-Steinfeld R, Schneider R, Amir G, Condiotti R, Heikenwalder M, Weber A, Schramm C, Wege H, Kluwe J, **Galun E***, Giladi H. (2016). Inflammation-Induced Expression and Secretion of MicroRNA 122 Leads to Reduced Blood Levels of Kidney-derived Erythropoietin and Anemia. Gastroenterology 151:999-1010. (* corresponding author)
Kleinschmidt D, Giannou AD, McGee HM, Kempski J, Steglich B, Huber FJ, Ernst TM, Shiri AM, Wegscheid C, Tasika E, Hübener P, Huber P, Bedke T, Steffens N, Agalioti T, Fuchs T, Noll J, Lotter H, Tiegs G, Lohse AW, Axelrod JH, **Galun E**, Flavell RA, Gagliani N, Huber S. (2017). A Protective Function of IL-22BP in Ischemia Reperfusion and Acetaminophen-Induced Liver Injury. J Immunol. 199:4078-4090.
Guedj A, Volman Y, Geiger-Maor A, Bolik J, Schumacher N, Künzel S, Baines JF, Nevo Y, Elgavish S, **Galun E**, Amsalem H, Schmidt-Arras D, Rachmilewitz J. (2019). Gut microbiota shape “inflamm-aging” cytokines and account for age-dependent decline in DNA damage repair. Gut 69:1064-1075

Benedek G, Abed El-Latif M, Miller K, **Galun E**, Levite M. Identification of the novel HLA-B allele, HLAB*15:539, in a South-Sudanese individual. **(**2019). HLA 94:380-381.

IL6 signaling: While investigating the inflammatory process in the liver upon injury we have detected IL6 as a central “player”. We have initiated a program to both understand the mechanism of how IL6 contributed to liver

regeneration, while at the same time developing a therapeutic approach of how utilizing this signaling to overcome major liver injury. It appears that IL6-transsignaling (TS) is a major contributor to the regenerative effects of IL6. We have recently also shown that IL6 TS overcomes senescence that is induced by radiation. This last effect is currently developed into a potential therapeutic platform. Salivary glands are at the radiation zone upon radiating head and neck tumors. The insult to the glands from radiation causes a dry mouth syndrome. We found that this is a result of senescence of the cells in the salivary gland. Pre-treating the salivary gland, by retrograde local administration of an IL6 designer protein that induces TS, prevents senescence and salivary loss of function, enabling salivation. We have also shown direct capability of leveraging our molecular techniques for detecting and assessing IL-6 for RF ablation studies.

Galun E, Zeira E, Pappo O, Peters M, Rose – John S. (2000). Liver regeneration induced by a designer human IL-6/sIL-6R fusion protein reverses severe hepatocellular injury. FASEB J 14: 1979-1987.
Hecht N, Pappo O, Shouval D, Rose-John S, **Galun E**, Axelrod JA. (2001). Hyper-IL-6 gene therapy reverses fulminant hepatic failure. Molecular Therapy 3: 683-687.
Nechemia-Arbely Y, Shriki A, Denz U, Drucker C, Scheller J, Raub J, Pappo O, Rose-John S, **Galun E**, Axelrod JH. (2011). Early Hepatocyte DNA Synthetic Response Posthepatectomy is Modulated by IL-6 Trans-Signaling and PI3K/AKT Activation. J Hepatology 54:922-9.
Marmary Y, Adar R, Gaska S, Wygoda A, Maly A, Cohen J, Eliashar R, Mizrachi L, Orfaig-Geva C, Baum B, Rose-John S, **Galun E**, Axelrod JH. (2016). Cellular Senescence Drives Radiation-Induced Loss of Salivary Gland Function and is Prevented by IL-6 Modulation. Cancer Res 76:1170-80.
Lanton T, Shriki A, Nechemia-Arbely Y, Abramovitch R, Levkovitch O, Adar R, Rosenberg N, Paldor M, Goldenberg D, Sonnenblick A, Peled A, Rose-John S, **Galun E**, Axelrod JH. (2017). IL6-Dependent Genomic Instability Heralds Accelerated Carcinogenesis Following Liver Regeneration on a Background of Chronic Hepatitis. Hepatology 65:1600-1611.
Moll JM, Wehmöller M, Frank NC, Homey L, Baran P, Garbers C, Lamertz L, Axelrod JH, **Galun E**, Mootz HD, Scheller J. (2017). Split2 protein-ligation generates active IL-6-type Hyper-cytokines from inactive precursors. ACS Synth Biol. 6:2260-2272.
Schmidt-Arras D, **Galun E**, Rose-John S. (2021). The two facets of gp130 signalling in liver tumorigenesis. Seminars in Immunopathology (in press).

Inflammation induced liver cancer: As a hepatologist one major interest I have is to develop drugs that will prevent or treat HCC. However, prior to developing such a therapeutic approach it is outmost important to understand the mechanism of inflammation induced HCC. We have identified pivotal factors through which the inflammatory process in the liver causes cancer. This is primarily NF-kB. We have adopted the Mdr2 knockout mice as the animal model in which we investigate the significance of the various inflammatory factors contributing to HCC following a prolonged inflammatory process. One pivotal cell, the macrophage, appears to be central to the development of HCC. We show that in a CCR5 knockout mice which prevent macrophage migration to the liver HCC is significantly attenuated. We also show that macrophages in the liver are central in DNA-damage response. We are now investigating the contribution of this to HCC development.

Abramovich R, Tavor E, Jacob-Hirsch J, Zeira E, Amariglio N, Pappo O, Rechavi G, **Galun E**, Honigman A. (2004). The pivotal role of CREB in tumor progression. Cancer Res 64:1338-46.
Pikarsky E, Porat RM, Stein I, Abramovich R, Amit S, Kasem S, Gutkovich-Pyest E, **Galun E**, Ben-Neriah Y. (2004). NF-kB functions as a tumor promoter in a mouse model of inflammation-associated liver cancer. Nature 43:461-6.
Barasa H, Gross E, Edrei Y, Israel A, Cohen I, Ben-Moshe T, Pappo O, Pikarsky E, Goldenberg D, Shiloh Y, **Galun E**, Abramovitch R. (2010). The accelerated carcinogenesis following liver regeneration is associated with chronic inflammation induced double strand DNA breaks. Proc Natl Acad Sci (USA) 107:2207-12.
Barashi N, Weiss ID, Wald O, Wald H, Beider K, Abraham M, Klein S, Goldenberg D, Axelrod J, Pikarsky E, Abramovitch R, Zeira E, **Galun E**, Peled A. (2013). Inflammation induced hepatocellular carcinoma is dependent on CCR5. Hepatology 58:1021-30.
Galun E. (2016). Liver inflammation and cancer: The role of tissue microenvironment in generating the tumor-promoting niche (TPN) in the development of hepatocellular carcinoma. Hepatology 63:354-6.

Simerzin A, Zorde-Khvalevsky E, Rivkin M, Adar R, Zucman-Rossi J, Couchy G, Roskams T, Govaere O, Oren M, Giladi H, **Galun E**. (2016). The liver-specific miR-122*, the complementary strand of miR-122, acts as a tumor suppressor by modulating the p53-Mdm2 circuitry. Hepatology 64:1623-1636.
Guedj A, Geiger-Maor A, **Galun E**, Amsalem H, Rachmilewitz J. (2016) Early Age Decline in DNA Repair Capacity in the Liver: In Depth Profile of Differential Gene Expression. Aging 8:3131-3146.
Stoyanov E, Mizrahi L, Olam D, Schnitzer-Perlman T, **Galun E**, Goldenberg D. (2017). Short-term S-adenosylmethionine supplementation suppresses tumor development in a murine model of inflammation-mediated hepatocarcinogenesis. Oncotarget 8:104772-104784.
Potikha T, Pappo O, Mizrahi L, Olam D, Maller SM, Rabinovich GA, **Galun E**, Goldenberg DS. (2019). Lack of galectin-1 exacerbates chronic hepatitis, liver fibrosis, and carcinogenesis in murine hepatocellular carcinoma model. FASEB J. 33:7995-8007.
Gamaev L, Mizrahi L, Friehmann T, Rosenberg N, Pappo O, Olam D, Zeira E, Halpern KB, Caruso S, Zucman-Rossi J, Axelrod JH, **Galun E**, Goldenberg DS. (2021). The pro-oncogenic effect of the lncRNA H19 in the development of chronic inflammation-mediated hepatocellular carcinoma. Oncogene 40:127-139.
Levite M, Safadi R, Milgrom Y, Massarwa M, **Galun E**. (2021). Neurotransmitters and Neuropeptides decrease PD-1 in T cells of healthy subjects and patients with hepatocellular carcinoma (HCC), and increase their proliferation and eradication of HCC cells. Neuropeptides (in press).

Shriki A, Lanton T, Sonnenblick A, Levkovitch-Siany O, Eidelshtein D, Abramovitch R, Rosenberg N, Pappo O, Elgavish S, Nevo Y, Safadi R, Peled A, Rose-John S, **Galun E***, Axelrod JH. (2021). Decisive Roles of IL-6 in Hepatic Injury, Steatosis, and Senescence Aggregate to Suppress Tumorigenesis. Cancer Res (in press).

Systemic tumorigenic effects of RF ablation: Most recently, we have developed an additional line of collaborative investigation into the secondary systemic effects of local thermal ablation that may contribute to unwanted 'off-target' stimulatory effects on distant tumor present elsewhere in the body. We have completed several studies characterizing post-ablation tumorigenic effects, including identifying key mechanisms responsible, such as periablational inflammation and growth factor production. Together with Profs. Ahmed and Goldberg of Boston, we have successfully combined RFA with adjuvant drug inhibitors of IL-6, c-Met, and VEGFR to block such tumorigenic effects. The following four publications support my expertise in the field.:

Rozenblum N, Zeira E, Scaiewicz V, Bulvik B, Gourevitch S, Yotvat H, **Galun E**, Goldberg SN. (2015). Oncogenesis: An "Off-Target" Effect of Radiofrequency Ablation. Radiology 276:426-32.
Ahmed M, Navarro G, Wang Y, Gourevitch S, Moussa MH, Rozenblum N, Levchenko T, Galun E, Torchilin VP, Ahmed M, Kumar G, Moussa M, Wang Y, Rozenblum N, **Galun E**, Goldberg SN. (2016). c-Met receptor inhibition can suppress hepatic radiofrequency ablation-induced stimulation of distant subcutaneous tumor growth. Radiology 279:103-17.
Bulvik BE, Rozenblum N, Gourevitch S, Ahmed M, **Galun E**, Goldberg SN. (2016). IRE versus RFA: A comparison of local and systemic effects in a small animal model. Radiology 280:413-24.
Kumar G, Goldberg SN, Wang Y, Velez E, Gourevitch S, **Galun E**, Ahmed M. (2016). Hepatic radiofrequency ablation: markedly reduced systemic effects by modulating periablational inflammation via cyclooxygenase-2 inhibition. Eur Radiol 27:1238-1247.
Kumar G, S. Goldberg NS, Gourevitch S, Levchenko T, Torchilin V, **Galun E**, Ahmed M. (2018). Targeting STAT3 to suppress systemic pro-oncogenic effects from hepatic RF ablation. Radiology 286:524-536.
Ahmed M, Kumar G, Gourevitch S, Levchenko T, **Galun E**, Torchilin V, Goldberg SN. (2018). Radiofrequency ablation (RFA) induced systemic tumor growth can be reduced by suppression of resultant heat shock proteins. Int J Hyperthermia 9:1-25.
Liao H, Ahmed M, MD, Markezana A, Zeng G, Stechele M, **Galun E**, Goldberg, NS. (2020). Thermal ablation induces time-dependent transitory intrahepatic metastatic growth via the STAT3/c-Met molecular pathway. Radiology 294:464-472.
Markezana A, Ahmed M, Kumar G, Zorde-Khvalevsky E, Rozenblum N, **Galun E**, Goldberg SN. (2020). Moderate hyperthermic heating encountered during thermal ablation increases tumor cell activity. Int J Hyperthermia 37:119-129.

The role of microRNAs in pathological and physiological conditions: It is becoming more and more apparent that microRNAs are functioning in metabolism, cancer and numerous other conditions. Our group recently generated data which actually shows that microRNAs act as hormones. They are expressed and secreted from one organ and function at a remote organ. We also show their effects in cancer other than HCC. We find that microRNAs are very cell lineage specific. These effects are expressed in the below reports:

Abraham M, Klein S, Bulvik B, Wald H, Weiss ID, Olam D, Weiss L, Beider K, Eizenberg O, Wald O, **Galun E**, Avigdor A, Benjamini O, Nagler A, Pereg Y, Tavor S, Peled A. (2017). The CXCR4 inhibitor BL-8040 induces the apoptosis of AML blasts by down-regulating ERK BCL-2, MCL-1 and cyclin-D1 via altered miR-15a/16-1 expression. Leukemia 31:2336-2346.
Chai C, Rivkin M, Berkovits L, Simerzin A, Zorde- Khvalevsky E, Rosenberg N, Klein S, Durst R, Shpitzen S, Udi S, Tam Y, Heeren J, Worthmann A, Schramm C, Kluwe J, Giladi H, **Galun E**. (2017). A Metabolic Circuit Involving Free Fatty Acids, MIR122 and Triglyceride Synthesis in the Liver and Muscle Tissues. Gastroenterology 153:1404-1415.
Chai C, Cox B, Yaish D, Gross D, Rosenberg N, Amblard F, Shemuelian Z, Gefen M, Korach A, Tirosh O, Lanton T, Link H, Tam J, Permikov A, Ozhan G, Citrin J, Liao H, Tannous M, Hahn M, Axelrod J, Arretxe E, Alonso E, Martinez-Arranz I, Ortiz Betés P, Safadi R, Salhab A, Amer J, Tber Z, Mengshetti S, Giladi H, Schinazi RF, **Galun E**. (2020). Agonist of RORA Reduces Progression of Fatty Liver in Mice via Upregulation of microRNA 122. Gastroenterology 159:999-1014.
Harari-Steinfeld R, Gefen M, Simerzin A, Zorde-Khvalevski E, Rivkin M, Ella E, Friehmann T, Gerlic M, Zucman Rossi J, Caruso S, Leveille M, Estall J, Goldenberg DS, Giladi H, **Galun E***, Bromberg Z. (2021). The lncRNA H19-derived microRNA-675 Promotes Liver Necroptosis by Targeting FADD. Cancers (in press).

Other collaboration, in which I contribute ideas and knowledge:
Birger A, Ben-Dor I, Ottolenghi M, Turetsky T, Gil Y, Sweetat S, Perez L, Belzer V, Casden N, Steiner D, Izrael M, **Galun E**, Feldman E, Behar O, Reubinoff B. (2019). Human iPSC-derived astrocytes from ALS patients with mutated C9ORF72 show increased oxidative stress and neurotoxicity. EBioMedicine 50:274-289.

Levite M, Zelig D, Friedman A, Ilouz N, Eilam R, Bromberg Z, Ramadhan Lasu AA, Arbel-Alon S, Edvardson S, Tarshish M, Riek LP, Lako RL, Reubinoff B, Lebendiker M, Yaish D, Stavsky A, **Galun E**. (2020). Dual-targeted Autoimmune Sword in Fatal Epilepsy: Patient's glutamate receptor AMPA GluR3 autoimmune antibodies bind, induce ROS, and kill both human neural cells and T cells. J of Autoimmunity (in press).

Benedek G, El Latif MA, Miller K, Rivkin M, Lasu AAR, Riek LP , Lako R, Edvardson S, Arbel-Alon S, **Galun E**, Levite M. (2020). Protection or susceptibility to devastating childhood epilepsy: Nodding Syndrome associates with immunogenetic fingerprints in the HLA binding groove. PLOS Neglected Tropical Diseases 14:e0008436.

Sadeh R , Sharkia I , Fialkoff G , Rahat A , Gutin J, Chappelboim A, Nitzan M , Ilana Fox-Fisher I , Neiman D, Meler G, Kamari Z , Yaish D , Peretz T , Hubert A, Cohen JE , Azzam S, Mark Temper M, Grinshpun A , Maoz M , Abu-Gazala S, Ben Yaacov A , Shteyer E, Safadi R, Kaplan T , Shemer R, Planer D , **Galun E** , Glaser B, Zick A, Dor Y , Friedman N. (2021). ChIP-seq of plasma cell-free nucleosomes identifies cell-of-origin gene expression programs. Nature Biotechnology (in press).

Benedek G, El Latif MA, Miller K, Rivkin M, Ramadhan AAL, Riek LP, Lako R, Edvardson S, Arbel Alon S, **Galun E**, Levite M. (2021). Macrophage migration inhibitory factor in Nodding Syndrome. PLoS Neglected Tropical Diseases (in press).

On-going Grants

Project Title	*Funding source*	*Amount (Euros)*	*Period*	*Role of the PI*

MicroRNA for HCC RxmiRcanceR #7865757	ERC Advance	3,000,000	2018-2023	PI 20%
IL6 signaling and transsignaling in HCC 2473/17	Israel Science Foundation	350,000	2017-2021	PI (10%)
The role of IL6 in NASH and HCC SFD 841 – C3	German Research Foundation (DFG)	400,000	2017 - 2022	Co-PI (5%)
NASH mechanism 486/17	Israel Science Foundation	400,000	2018 - 2022	PI (10%)

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