RESEARCH BULLETIN

DR. SHIGEMI ISHIKAWA-NAGAI RECEIVES CATALYST AWARD FROM THE NATIONAL ACADEMY OF MEDICINE

Shigemi Ishikawa-Nagai, DMD, PhD, associate professor of Oral Medicine, Infection and Immunity and director of clinical research at HSDM, received the Catalyst Phase Award from the National Academy of Medicine’s Healthy Longevity Global Competition.

The project, “A Novel Paradigm for Blood Brain Barrier-Independent Molecular Passage to Brain: Retrograde Axonal Transit of Craniofacial tissue Exosome (RATCE),” is a collaboration with co-investigators Masazumi Nagai, DDS, PhD, lecturer on Oral Medicine, Infection, and Immunity, Albert Galaburda, MD, Emily Fisher Landau, professor of Neurology and Neuroscience, Harvard Medical School, co-director, Mind Brain Behavior Interfaculty Initiative, Harvard University, senior neurologist, Department of Neurology, and John Da Silva, DMD, MPH, ScD, associate professor of Restorative Dentistry and Biomaterials Sciences and vice dean of HSDM.

The origin of this project is based on prosthodontics and our multidisciplinary research team has been working on the association between healthy masticatory function and cognitive health. Along with life expectancy, age-associated Alzheimer’s disease (AD) has been increasing. While dysfunction of the blood-brain barrier (BBB) may contribute to AD, the BBB also limits the passage of beneficial molecules. Alternative routes into the brain remain to be explored. Dr. Nagai and colleagues previously reported that masseter muscle packaged neprilysin, which breaks down amyloid β in exosomes and sends them to the hippocampus by retrograde axonal transport along trigeminal nerve, bypassing the BBB. The direct central nerve-innervation exceptionally occurs in craniofacial tissues (CFT) such as masseter/facial expression/tongue-muscles, periodontal fibroblasts, submandibular gland cells, and dental pulp cells. Every CFT can also transport neuroprotective agents to the brain through RATCE. The first aim of this project is to identify neuroprotective RATCE cargo through comparative mRNA transcriptome profiling between hippocampal neuron cells and CFT cells with glial astrocytes as a positive competitor owing to their neuroprotective functions. Proteins corresponding to neuron-negligible and CFT/glial-dominant mRNA transcripts will be validated in corresponding exosomes and hippocampal neuron as the RATCE cargo. The cargo comparison between CFT and glial astrocytes will shed light on the significance of RATCE. The second aim is to compare the therapeutic efficacies of RATCE with conventional intravenous and body muscle injections on AD onset in the amyloid-based disease model mice. This project offers a paradigm-shifting innovation in the physiological maintenance of brain homeostasis and therapeutic drug delivery through the BBB-independent RATCE pathways.

Photographed (left to right) are Drs. Albert Galaburda, Masazumi Nagai, and John Da Silva
PUBLICATIONS

DEVELOPMENTAL BIOLOGY


ORAL MEDICINE, INFECTION AND IMMUNITY


Lamont E, Hendrickson E, McLean J, He X, Bor B. Complete genome sequence of strain BB001, a novel epibiont bacterium from the candidate phylum Saccharibacteria (TM7). Microbiology Resource Announcements 2020 Aug;9(34).

Li C, Almazrooa S, Carvo I, Salcines A, Woo SB. Architectural alterations in oral epithelial dysplasia are similar in unifocal and proliferative leukoplakia. Head and Neck Pathology 2020; Sep 16.


ORAL AND MAXILLOFACIAL SURGERY


ORAL HEALTH POLICY AND EPIDEMIOLOGY


Chandrupatla S, Khalid I, Muthuluri T, Dantala S, Tavares M. Diabetes and prediabetes prevalence among young and middle-aged adults, and geographic differences in India- National Family Health Survey. Epidemiology and Health 2020;e2020065.


Hackley D. Climate change and oral health. International Dental Journal 2020; Sep 25.
ORAL HEALTH POLICY AND EPIDEMIOLOGY


RESTORATIVE DENTISTRY AND BIOMATERIALS SCIENCES


MULTI-DEPARTMENTAL


AWARDS & RECOGNITIONS

Gili Naveh, DMD, PhD, assistant professor of Oral Medicine, Infection and Immunity and Andy Lee, DMD, DMSc candidate in Oral Biology 2021 and member of the Naveh Lab, received the 2020-2021 Simmons Award from the Harvard Center for Biological Imaging for “The Dense Collar as a Structural Barrier to Bacterial Invasion into PDL.” Thanks to a generous donation from Dr. and Mrs. Daniel Simmons, the HCBI offers grants to offset the costs of imaging in the facility.

Thomas Nguyen, DMD, instructor in Oral Medicine, Infection and Immunity, received the American Association of Periodontology Foundation Nevins Teaching and Clinical Research Fellowship and Nevins BioHorizons Fellowship. This two-year fellowship will support Nguyen’s academic career and aims to keep periodontology at the cutting edge of scientific dentistry. We wish Dr. Nguyen all the best as he is departing HSDM to join the Faculty of Dentistry at McGill University in Montreal, Canada.

Shaikha Aldukhail, BDS, DMSc, DMSc candidate in Dental Public Health 2021, received first place in the 2020 American Institute of Dental Public Health Mini Colloquium Student Poster Contest, sponsored by the American Dental Association. Her project, “Oral Health Outcomes Among Diabetic Adult Patients Served at HRSA-Funded Health Centers” was completed with Hesham Alhazmi, BDS, MS, DMSc candidate in Dental Public Health as well as Christine A. Riedy, PhD, MPH; Jane R. Barrow, MS; and, Steffany Chamut, DDS, MPH, in the Department of Oral Health Policy and Epidemiology.
Hend Alqaderi, BDS, DMSc, lecturer on Oral Health Policy and Epidemiology at HSDM and Assistant Clinical Investigator at the Forsyth Institute, received a Forsyth Institute Special Grant on COVID-19 Research. Dr. Alqaderi is principal investigator of the study, “Salivary Cytokine Levels in Symptomatic and Asymptomatic Patients with COVID-19.” The co-principal investigator in Kuwait is Dr. Saadoun Bin-Hasan.

The immune response to SARS-CoV2 involves multiple processes and cellular mechanisms representing a complex pathology. “Cytokine Storm” has been suggested as a critical and pathogenetic landmark of SARS-CoV2 infection and COVID-19 and refers to the elevated levels of cytokines associated with a wide array of cellular and molecular phases of immunity. Even though there is emerging evidence showing that the severity of the symptoms of patients with COVID-19 may be associated with elevated cytokines, there is a lack of knowledge on whether the levels of these salivary molecules demonstrate any correlation with the clinical symptoms.

Saliva provides a non-invasive and abundant diagnostic platform for detection of cytokines associated with deviations from health with a predictive capacity of disease processes. Alqaderi’s work has demonstrated the utility of saliva as a non-invasive biomarker detection tool in a pediatric cohort of Kuwaiti children.

This project will further the understanding of potential cytokines associated with different levels of infection and provide information on why a subset of individuals are prone to develop severe disease while the majority of SARS-CoV2 infected individuals are asymptomatic. Additionally, this study will provide preliminary results on the possibility of using saliva as a tool to predict the severity of the symptoms.