Session 1

Thomas Jefferson University. What we are, What we do

Ignazio R. Marino, MD, ScD

Professor of Surgery, Sidney Kimmel Medical College, Thomas Jefferson University
Strategic Advisor to the President & CEO, Thomas Jefferson University and Jefferson Health
Philadelphia, PA, United States of America

ignazio.marino@jefferson.edu

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We are Jefferson

Jefferson.edu / JeffersonHealth.org

- Home of Thomas Jefferson University and the Sidney Kimmel Medical College
- 9 colleges and 4 schools spanning medicine, science, architecture, design, textiles, business, engineering and more
- 160 undergraduate/graduate programs
- 7,800 students, 1,070 medical student rotations, 1,300 residents and fellows
- Ranked by U.S. News & World Report as the nation's 16th Best Hospital
- Nationally ranked in 11 clinical specialties
- Includes 13 hospitals, 2,824 beds, 6,000 physicians, 7,200 nurses
- 50+ outpatient and urgent care locations
- 3.6 million patient interactions and 3 million outpatient visits
- NCI-designated Sidney Kimmel Cancer Center
- Over 110 million USD in public/private research funding

Among the Top 10 in the U.S.

- Ear, Nose & Throat
- Ophthalmology
- *Orthopedics*

Nationally Ranked Specialties

- *Cancer*
- Cardiology & Heart Surgery
- Diabetes & Endocrinology
- Gastroenterology & GI Surgery
- Geriatrics
- Nephrology
- *Neurology* & Neurosurgery
- *Urology*

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Topic

Jefferson is seeking Coordination and/or Partnership on the following Horizon 2020 SC1 topics

SC1-BHC-04-2018	**Rare Disease European Joint Programme Co-Fund**
SC1-BHC-18-2018	**Translational collaborative cancer research between Europe and** the Community of **Latin American and Caribbean States** (CELAC)
SC1-BHC-09-2018	**Innovation Platforms for Advanced Therapies of the Future**
SC1-HCO-04-2018	ERA-NET to support the **Joint Programming in Neurodegenerative Diseases**
strategic	plan (JPND)
SC1-BHC-02-2019	System **Approaches for the Discovery of Combinatorial Therapies** for Complex Disorders

and on the following projects

- "**Rabies Virus-Based Vector** (RABV) **Vaccine Platform**"
- "**Febrile Seizures as a marker of sudden death in children**"

Keywords

Epidermolysis bullosa, rare heritable skin diseases, prostate cancer, artificial intelligence, spine injury, cannabinoids, Parkinson's disease, vaccines, Rabies Virus-based Vector Vaccine, Ebola virus, Lassa fever virus, MERS-CoV, SARS-CoV, Nipah virus, Rift Valley fever virus, Amyotrophic Lateral Sclerosis, sudden cardiac death, Brugada syndrome, febrile seizures.

Proposed study: Proposal for Multinational Co-operative Research Program on Epidermolysis Bullosa as a Paradigm of Rare Heritable Skin Disorders

Aim: **to study an orphan disease such as Epidermolysis bullosa** (EB) for new diagnostic means, development of animal models and preclinical treatment development culminating in clinical trials for rare diseases.

Program Development

- **Development of advanced next generation sequencing platforms towards identification of novel genes** and new mutant alleles
- Development of animal models for different types of EB by advanced CRISPR/Cas9 technology
- Utilization of mouse models for preclinical treatment development within the realm of precision medicine based on identification of specific mutations
- **Clinical trials to test novel treatments based on information emanating from the preclinical rodent studies**
- **Formalization of patient registries in Europe and in the U.S. with exchange of phenotypic and genotypic information**

International Consortium

- Istituto Dermopatico dell'Immacolata, Rome, ITALY
- Bambino Gesù Pediatric Hospital, Rome, ITALY
- Department of Dermatology, Freiburg Medical Center, Freiburg, GERMANY
- Paracelsus Medical University, EB-Haus, Salzburg, AUSTRIA
- Department of Dermatology and Cutaneous Biology, Jefferson, Philadelphia, PA, USA

Lead Jefferson's investigator: Jouni Uitto jouni.uitto@jefferson.edu

SC1-BHC-04-2018

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Proposed study: A Novel, Non-invasive, Urinary Assay for Early Detection of Prostate Cancer (Pca)

The era of molecular profiling has led investigators to new discoveries in the field of PCa. **Our goal is** to adapt, validate and translate these findings into **a clinically useful and a commercially viable assay**.

Aims

1.To determine sensitivity, specificity, positive predicative value (PPV) and negative predicative value (NPV) of the **urinary assay** for detection of PCa;
2.To determine the use of the **urinary assay** in the management of patients with recurrent PCa after radiotherapy;
3.To determine the use of the **urinary assay** in the management of patients with persistently elevated PSA and negative prostate biopsy;
4.To determine if the detected malignant cells as a % total number of cells shed in urine correlate with the severity of the disease.

Additional applications

i. **Use for screening test (553M male >65 yrs worldwide for 55.5M in US and EU)**
ii. Monitor the PCa status on those male on surveillance
iii. Determine effectiveness of therapeutic intervention
iv. **Minimize unnecessary prostate biopsies (1.2M/year in the USA alone)**
v. **Spare patients from unneeded trauma and save billions of healthcare money**

International Consortium

- Department of Nuclear Medicine, Docrates Cancer Center, Helsinki, FINLAND
- Nuclear Medicine and Biophysics, University Hospital of Martinique, FRANCE
- Marcus Institute of Integrative Medicine, Thomas Jefferson University, Philadelphia, PA, USA
- Laboratories of Radiopharmaceutical Research and Molecular Imaging, Thomas Jefferson University, USA

Lead Jefferson's investigator: Mathew Thakur madhukar.thakur@jefferson.edu

SC1-BHC-18-2018

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Proposed study: Development of Artificial Intelligence Systems for AOSpine Injury Classification (AIS-AOS)

We propose to develop a computer-aided diagnosis system named AIS-AOS employing deep learning techniques **originating from the field of artificial intelligence** (AI) such that **an automated injury classification of spinal traumas** can be provided **based on regular CT-scan images**.
Specifically, the AIS-AOS will provide:
1) automatic classification and localization of the thoracolumbar vertebral fractures caused by trauma according to AOSpine classification system and
2) automatic segmentation and labeling of the vertebrae in CT images.

Major benefits: **the classification of trauma patterns could be faster and more reliable**; trauma surgeons with less experience in the biomechanics and pathology of the complex spinal column will be able to provide adequate care. **This project also shows the way for the development of a productive joint venture between surgeons and high-tech world.**
500-1000 cases will be used as datasets to analyze.
At the end of the project an AIS-AOS software package will be available as a first release.

International Consortium
- AOSpine Knowledge Forum Trauma, AO Foundation, Davos, SWITZERLAND
- Image Sciences Institute and the Department of Orthopedics, UMC Utrecht, NETHERLANDS
- Rothman Institute at Jefferson, Philadelphia, PA, USA https://www.rothmaninstitute.com/

Lead Jefferson's investigator: Alex Vaccaro alex.vaccaro@rothmaninstitute.com

SC1-BHC-09-2018

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Proposed Study: Attacking Disease-Driven Pharmaco-resistance in Amyotrophic Lateral Sclerosis (ALS). A Personalized and Combinatorial Therapeutic Strategy to Enhance Delivery and Efficacy of ALS Therapeutics

Preamble

In Europe, ALS kills more than 8,000 people annually with health care costs of 596 million euro. Jefferson has been the first group to identify drug-efflux transporters-driven pharmaco-resistance in ALS and to characterize its negative impact on drug delivery.

Aim

To **study the role played by** P-gp and BCRP **drug efflux transporters in limiting the development of effective treatments for ALS**. **The ultimate goal is to develop** and characterize P-gp/BCRP **inhibitors to be used in combination with ALS therapeutics, starting with Riluzole, in order to enhance their efficacy in patients**.

Project development

Phase 1 - P-gp/BCRP as ALS Biomarkers: Towards Personalized Medicine in ALS Patients
Phase 2 - Riluzole: a Proof-of-Principle Drug to Develop a Combinatorial Therapy for ALS
Phase 3 - Blocking and Tracking Pharmaco-resistance in ALS Patients: An International Multi-Center Clinical trial

International Consortium

- Vickie and Jack Farber Institute for Neuroscience, Weinberg ALS Center, Thor
- ALS Center, University of Turin, Turin, ITALY
- Vesalius Research Center, University of Leuven, BELGIUM

Lead Jefferson's investigator: Piera Pasinelli piera.pasinelli@jefferson.edu

SC1-BHC-02-2019

(also **IMI** Improving Preclinical Prediction of Adverse Effects of Pharmaceuticals in the Nervous System; or **Pilot Program on Clinical Compound Bank for Repurposing;** Neurodegenerative Diseases)

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Proposed study: Cannabinoids as Therapy in Parkinson's Disease (PD)

- **3 year long, randomized controlled study, 2 arms with 3 groups within each arm**
- At each collaborating center, 75 patients enrolled into each arm (25/group)

Arm 1 Early stage PD patients; ≤ 2 years from diagnosis; score <2 on the Hoehn and Yahr (H&R) scale; no PD-modifying medications. Goal: to measure effects of cannabinoids on pain and tremor and evaluate their disease-modifying potential.

Arm 2 Mid-stage PD patients; score 3-5 on H&R scale; 5-15 years of L-dopa therapy; sustained L-dopa induced dyskinesias. **Goal: to examine the ability of cannabinoids to modify or reduce dyskinesias and collect data on non-motor symptom effects**.

Additional social and economic study aspects

Surveys and interviews of patients and caregivers regarding alteration of their perception of PD and ease of care; assessment of whether cannabinoids impact hospitalization rates, ambulatory care costs, drug costs.

International Consortium

- Department of Neurological Sciences, Università Tor Vergata, Roma, ITALY
- Hebrew University, Jerusalem, ISRAEL
- The Lambert Center for the Study of Medicinal Cannabis and Hemp, Thomas Jefferson University, USA

Lead Jefferson's investigator: Charles Pollack charles.pollack@jefferson.edu
http://www.jefferson.edu/lambertcenter

SC1-HCO-04-2018

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Proposed Study: Rabies Virus-Based Vector (RABV) Vaccine Platform

Aim

To further develop our deactivated RABV vector vaccine platform and produce and charcterize RABV-based vaccines against Lassa fever virus, MERS-CoV, SARS-CoV, Nipah virus vaccines.

Jefferson has established a world class consortium which can rapidly develop, test and manufacture new vaccines against emergent pathogens and move them into clinical trials. **NIH currently supports the development of the RABV-based vaccine against Ebola virus, Sudan virus and Marburg virus vaccine with $ 30 million**.

- **We would propose** to produce and store MVS of vaccines against viral pathogens with a high potential to emerge as serious health threats of large population groups.
- We will establish, and have in place, **a fast track system to clone and recover new constructs for novel identified pathogens within weeks of a new disease threat being identified** and shortly thereafter provide well characterized MVS utilizing novel technology such as deep sequencing.
- We will work closely with a BSL4 laboratory in parallel to analyze such novel vaccines against those new emerging pathogens in the appropriate animal models utilizing the required biosafety level and skills (e.g. BSL4).
- We have partners to move the novel vaccine rapidly thought clinical phase 1, 2 and 3.

International Consortium

- IDT Biologika GmbH, GERMANY
- QuintilesIMS (now IQVIA), Clinical trial with multiple offices in Europe
- Jefferson Vaccine Center, Thomas Jefferson University, Philadelphia, PA, USA

Lead Jefferson's investigator: Matthias Schnell matthias.schnell@jefferson.edu

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Proposed study: Febrile Seizures as a marker of sudden death in children

Aim: **To determine whether testing children with febrile seizures for inherited channelopathies** (ie long QT syndrome and/or Brugada syndrome) **facilitates early identification of a cohort of children and family members at high risk of malignant arrhythmia syndromes**.

Significance: **There are no current standards for ECG and follow up testing for children presenting with febrile seizures to identify malignant arrhythmia syndromes**. **Febrile seizures may be a missed opportunity to identify these syndromes**. **While universal screening is not practical, targeted screening of patients with a febrile seizure, which is more common and may present earlier than sudden cardiac death (SCD), may represent an important opportunity to identify and treat the rarer causes of SCD**. **The results will be used by emergency physicians, pediatricians, neurologists, and cardiologists who care for children with febrile seizures**.

Program Development

a) Identify European study sites that see a sufficient number of children with febrile seizures. (total n=360)

b) Compare cohorts of children at each institution: (1) children with febrile seizures, (2) non-sibling children without fever or seizure who are being seen in the Emergency Departments, (3) children with fever without a seizure, and (4) children with seizure without a fever

c) Enroll subjects and collect data including blood and genetic testing

d) Data analysis and dissemination

International Consortium

- Cardiology Department, St. Joan de Déu Hospital, Barcelona, SPAIN
- Department of Emergency Medicine, Thomas Jefferson University, Philadelphia, PA, USA

Lead Jefferson's investigator: Jennifer White jennifer.white2@jefferson.edu

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GENERAL INQUIRIES ignazio.marino@jefferson.edu

RARE HERITABLE SKIN DISEASES, EPIDERMOLYSIS BULLOSA jouni.uitto@jefferson.edu

PROSTATE CANCER LIQUID BIOPSY madhukar.thakur@jefferson.edu

ARTIFICIAL INTELLIGENCE FOR SPINE INJURIES alex.vaccaro@rothmaninstitute.com

CANNABINOIDS AND PARKINSON'S DISEASE charles.pollack@jefferson.edu

PHARMACO RESISTANCE IN ALS piera.pasinelli@jefferson.edu

RABIES VIRUS-BASED VECTOR VACCINE PLATFORM matthias.schnell@jefferson.edu

FEBRILE SEIZURE, SUDDEN CARDIAC DEATH jennifer.white2@jefferson.edu

http://www.jefferson.edu/ http://www.jeffersonhealth.org/

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