

PhD Position: Program INPhINIT Fundació La Caixa

Role of myosteatorsis in the occurrence and persistence of residual muscle weakness in acromegaly and Cushing's syndrome. Study of the mechanisms involved

(Dr.Susan Webb)

CENTRE: IIB SANT PAU - Fundació Institut de Recerca de l'Hospital de la Santa Creu i Sant Pau

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CENTRE DESCRIPTION:

The Research Institute of the Hospital de la Santa Creu i Sant Pau (HSCSP-IR) was created on 4 June 1992 as a private scientific foundation. Its mission is to promote basic, clinical, epidemiological and healthcare research in the health science and biomedical fields, with the ultimate aim of improving the health of the population. On 10 December 2003, the Autonomous Government of Catalonia approved affiliation of the HSCSP-IR as a University Research Institute attached to the Autonomous University of Barcelona (UAB).

The HSCSP-IR has as its mission to improve the health and quality of life of the population through the production and dissemination of scientific knowledge, the training of researchers to an international standard, innovation in health and the incorporation of medical advances in clinical practice and in healthcare policies.

The HSCSP-IR is currently one of the most active research centres in Catalonia, especially in relation to translational research and the application of new discoveries to clinical practice. Since 2011 it has been part of the Catalan System of Research Centres (CERCA).

On 17 May 2009, the HSCSP-IR and nine other organizations created the Sant Pau Biomedical Research Institute (IIB Sant Pau), with the aim of strengthening collaborative translational research and bridging the gap between basic research and clinical practice so as to ultimately improve patient care.

AREA OF KNOWLEDGE: Life Sciences Panel

GROUP LEADER: Dr. Susan Webb / swebb@santpau.cat



RESEARCH PROJECT/RESEARCH GROUP

The research group "Pituitary diseases" is part of the research institute of the Hospital Sant Pau

<http://www.recercasantpau.cat/es/grupo/enfermedades-hipofisis/>

POSITION DESCRIPTION

-Research Project / Research Group Description:

Cushing's Syndrome and acromegaly determine myopathy and muscle weakness which persist after remission of hormone excess. Fatty infiltration in skeletal muscle is associated with atrophy, frailty, and increased metabolic morbidity and mortality. Muscle MRI using T2 mapping & 3-point Dixon imaging studies quantify the degree of fat infiltration and allows a sensitive determination of muscle structural characteristics, including necrosis, inflammation and edema. Ultrasound measurement of the rectus femoris cross-sectional area is a marker of muscle strength. Several molecules regulate the interplay between fat and the musculoskeletal system. Adiponectin stimulates muscle regeneration and inhibits fat accumulation; myostatin induces bone marrow mesenchymal differentiation to adipogenesis at the expense of osteoblastogenesis, and Dickkopf-1 (DKK-1) inhibits bone formation which is negatively associated with muscle contraction. MicroRNAs are small non coding RNA that might act as positive/negative regulators of muscle atrophy. Some miRNAs are associated with muscular strength in humans and in vitro studies have shown that glucocorticoids (GC) and growth hormone (GH) modulates the expression of several miRNAs involved in the regulation of muscle performance. Aims: Evaluate myosteatosis with MRI (T2 mapping & 3-point Dixon) and muscle cross-sectional area with ultrasound, and correlate with muscle functional tests; assess cytokines and miRNA that mediate the interaction between fat and musculoskeletal system in CS and acromegaly, where body composition is abnormal. Investigate these muscle-fat relationships would may pave the path in the allow the search of therapeutic targets for muscle weakness which persists as, residual morbidity after correction of GC and GH excess in patients with rare conditions like CS and acromegaly, which share similarities with sarcopenia and bone frailty, characteristic of aging.

-Job position description:

Clinical research means working directly with patients and can only be performed in academic hospitals. Clinical observations lead the research questions, in this case explain why patients endocrinologically cured from the hypersecretion of GH (acromegaly) or GC (CS), still complain of muscular fatigue and have more fractures. My responsibilities include identifying and contacting potential participants from the patient databases in Sant Pau hospital, a reference

centre for pituitary diseases; if interested, I set up appointments and explain the study prior to the patient signing an informed consent, approved by the Ethics Committee. Additionally, I look for a matched healthy control, from the blood donors or cohort of controls recruited over the years, whom I then contact.

I arrange for blood tests, imaging studies and physiotherapy appointments and collect clinical, anthropometric and analytical/imaging data in a specific database designed under the leadership of the PI. I arrange for the shipment of samples for micro RNA measurements, to CEO EpiDisease S.L. in Valencia. I collect copies of MRIs on a CD, for post-processing with Point 3 Dixon by the neurologist; lumbar CT scans used to establish bone distribution and volumetric and biomechanical characteristics will be provided to the bone specialist in charge of the software required for this analysis. I will perform statistical analysis prior to communication of results at meetings and write manuscripts for endocrine journals of 1st/2nd quartile of "Endocrinology & Metabolism". This will be my PhD thesis.

Frequent meetings and contacts with the research team (endocrinologists, radiologists, neurologist, physiotherapist, molecular biologists, bone specialist, etc.) will guarantee that any deviation from the protocol or unresolved problems are promptly approached to guarantee the success of the project. I will also participate in educational/ training workshops and seminars, to complement my research training

OTHER RELEVANT WEBSITES

The research group is also a CIBERER group (Network of Excellence of Rare Diseases, group number 747. The PI of both these groups is S Webb:

<https://www.ciberer.es/grupos/grupos-de-investigacion?grupos=U708,U712,U747,U725A>

