

P393**DISSECTING THE MOLECULAR MECHANISMS BEHIND THE BIOSYNTHESIS AND TRAFFICKING OF THE CALCIUM-SENSING RECEPTOR**L. Jamartino¹, M. L. Brandi²¹Dept. of Experimental & Clinical Biomedical Sciences, University of Florence, ²Dept. of Experimental & Clinical Biomedical Sciences, University of Florence; FIRMO Foundation, Florence, Italy

The calcium-sensing receptor (CaSR) is a GPCR receptor that controls calcium level in the blood by regulating the synthesis and the secretion of PTH. Defects on CaSR activity, due to its downregulation or to inherited mutations, lead to hyperparathyroidism disorders and to calcium/PTH imbalance. It appears, despite some contradictory reports, that pharmacological stimulation of the CaSR *via* its specific FDA-approved modulator cinacalcet increases CaSR expression and its membrane recruitment. However, the mechanisms behind CaSR biosynthesis and its anterograde trafficking are still unclear and require further proofs.

The aim of the present study is to dissect how CaSR activation triggers its own biosynthesis and whether this can be further enhanced by pharmacological stimulation.

Using either bovine parathyroid and human adenoma parathyroid cells, either HEK cells stably transfected with a CaSR-expressing vector (HEK_CaSR), we are investigating the changes of CaSR expression and signaling via RT-qPCR, western blot, IP-one and intracellular calcium mobilization assays. We are further double transfecting the parathyroid cell line (PTH1C1), generated in our laboratory, with vectors expressing CFP-tag CaSR and DKK-tag PTH. With this model we will be able to i) monitor CaSR biosynthesis and membrane trafficking through live cell imaging; ii) CaSR activity by assessing PTH production and secretion; iii) assess the interaction of the CaSR with down-stream signaling factors via immunoprecipitation and further unveil novel interacting proteins through mass spectrometry and FRET assays.

Our preliminary data show that in HEK_CaSR cells, 24 h stimulation with 1 μM of cinacalcet increases CaSR mRNA and protein levels by 2-fold compared to untreated control, while inhibiting the CaSR with 1 μM of NPS 2143 reduces CaSR expression.

Based on our early results, we suggest the existence of a positive feedback mechanism that promotes CaSR biosynthesis upon its stimulation. Commonly GPCRs internalize once activated causing desensitization, while the CaSR seems to guarantee a sustained signaling upon continuous stimulus. Exploiting this mechanism will allow us to improve current pharmacological treatments for hyperparathyroidism disorders.

P394**AN ASSESSMENT OF THE TOULOUSE SAINT LOUIS UNIVERSITY MINI FALLS ASSESSMENT TOOL TO PREDICT INCIDENT FALLS AMONG OLDER ADULTS RESIDING IN NURSING HOMES: A 6-MONTH PROSPECTIVE STUDY**M. Locquet¹, F. Bonnard¹, C. Beaudart¹, C. Coendo², S. Gillain³, J.-Y. Reginster¹, O. Bruyère¹¹University of Liège, Division of Public Health, Epidemiology and Health Economics, ²University Hospital of Liège, Physical Rehabilitation Medicine and Sports Traumatology, ³University Hospital of Liège, Geriatrics Dept., Liège, Belgium

Objectives: Toulouse Saint Louis University Mini Falls Assessment (TSLUMFA) tool has been designed to predict falls. It was initially validated in a geriatric clinic in 2018. The primary objective was to evaluate the predictive capacity of the TSLUMFA for incident falls in older adults residing in nursing homes. The secondary objective was to determine the TSLUMFA optimal cut-off value identifying those older adults with a high-risk of falling.

Methods: Settings: A longitudinal study was carried out over a period of 6 months. Participants: 93 older adults residing in nursing homes were

evaluated for the present study. Measurements: The TSLUMFA (made up of 7 criteria) was administered at baseline, and incident falls were recorded based on a registry of falls. Comparisons of TSLUMFA scores between fallers and non-fallers were performed using the U Mann-Whitney test or χ^2 . Correlation between the total TSLUMFA score (/30 points) and incident fall(s) was explored using the Cox proportional hazard model. ROC analysis enabled an optimal cutoff value to be established to identify those adults at the highest risk of falling.

Results: In the study, 93 older adults (61.3% women) with a median age of 80 (69-87) y were included. The median total TSLUMFA score was 21 (19-24.5) points. During the 6-month study period, 38 subjects (40.9%) experienced at least one fall. The total TSLUMFA score in older adults with incident fall(s) was significantly lower than in those who did not fall (20 (15.75-22.25) points vs. 23 (20-25) points and a p-value of <0.001). For each 1-point higher score at the total TSLUMFA a 9% less chance of falling was observed during the study period (p-value=0.006). The AUC was 0.736 (95%CI: 0.617-0.822) and p-value<0.001, clearly demonstrating its interesting performance as a screening tool. A score of ≤ 21 points was identified as the optimal cutoff to identify those older adults at a higher risk of falling.

Conclusion: The TSLUMFA performed well and successfully identified older adults with a high risk of falling in a nursing home setting. Further comparisons with existing tools are warranted.

P395**EMPLOYMENT RETENTION AMONGST HIP ARTHROPLASTY RECIPIENTS WHO RETURN TO WORK**E. Zaballa¹, G. Ntani¹, E. C. Harris¹, A. Lübbecke-Wolff², N. K. Arden³, C. Cooper⁴, K. Walker-Bone¹¹MRC Versus Arthritis Centre for Musculoskeletal Health and Work, University of Southampton, Southampton, UK, ²Division of Orthopaedics and Trauma Surgery, Geneva University Hospitals, Geneva, Switzerland, ³Centre for Sport, Exercise and Osteoarthritis Research Versus Arthritis, University of Oxford, Oxford, UK, ⁴MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, UK

Objective: To explore associations between exposure to physically demanding work performed after total hip arthroplasty (THA) and job loss due to the replaced hip.

Methods: A postal survey was mailed to THA recipients from the Geneva Hip Arthroplasty Registry and the Clinical Outcomes in Arthroplasty study. To be eligible, patients needed to have received their arthroplasty at least 5 y before and to have been aged 18-64 y at the time. Data collection included: demographics, time to reach best function and postoperative recreational activities. For each job held postoperatively, participants self-reported exposure to a range of physically demanding activities (standing, walking, kneeling/squatting, climbing ladders, digging). Cox proportional hazard models were used to estimate the effect of occupational activities on the risk of job loss.

Results: Of the 817 respondents (57% response rate), 514 returned to work (RTW) postoperatively. The median follow-up post-THA was 7.5 y (IQR 6.2 -12.1). Occupational exposure information was available for 411 of the 514 who RTW (206 men, 205 women). Adjusted models (age at operation, sex, BMI, time to reach best postoperative function, cohort and follow-up) showed an increased risk of stopping work post-THA in workers who needed to stand >4 h/d (HR:3.81, 95%CI 1.62-8.96); kneel/squat (HR:95%CI 3.32, 1.46-7.55) and carry/lift >0 kg (HR:5.43, 95%CI 2.29-12.88) compared with those who did not. Mutually adjusted models showed that the effect of lifting/carrying weights in excess of 10 kg remained statistically significant (p<0.01).

Conclusion: Jobs that entail standing, kneeling/squatting or lifting heavy weights are more difficult to retain amongst THA recipients. These findings need to be confirmed in other cohorts, but clinicians may need to