

Since July 2021, a cohort exceeding 100 Long Covid patients has been identified during family medicine consultations in Charleroi, Belgium. The diagnosis of Long Covid, characterized by a constellation of medically unexplained symptoms, is predominantly reliant on clinical assessment. Conventional biological examinations and imaging studies yield no fruitful findings. In instances of severe presentation, cognitive dysfunction has prompted the utilization of single-photon emission computed tomography (SPECT CT), a modality capable of detecting anomalies in cerebral blood perfusion. Furthermore, through collaboration with the Covid Human Genetic Effort network, comprehensive multi-omics investigations have been conducted at REGA Institute, Leuven, Belgium.

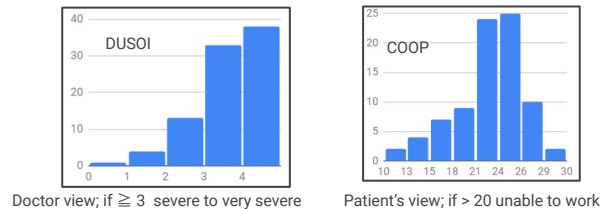
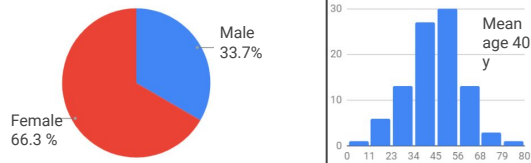
## Methods;

Cohort of PACS patients identified during clinical encounters in family medicine.  
Identification of a set of medically unexplained symptoms as PACS  
Evaluation of the severity (DUSOI\*) by the doctor  
Evaluation of the health status by the patient (COOP Charts\*\*)  
If DUSOI ≥ 3 and COOP >20 → SPECT-CT ordered  
All PACS patients → blood sample → transcriptomic studies at REGA institute, Leuven.  
Ethical agreement by KUL and ULg ethical committees

**Qualitative results; bag of words, patient's wording, 34 first patients verbatim**

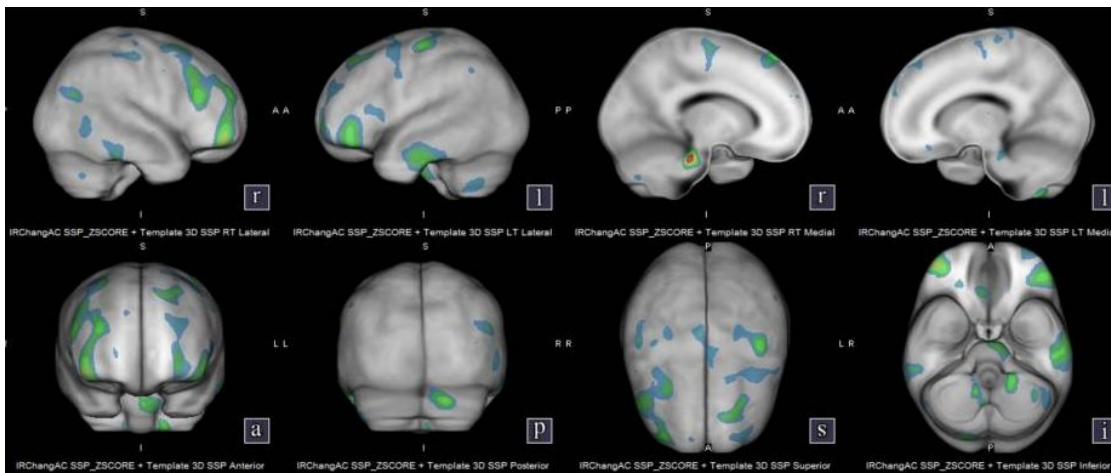


## Results; data on 102 patients



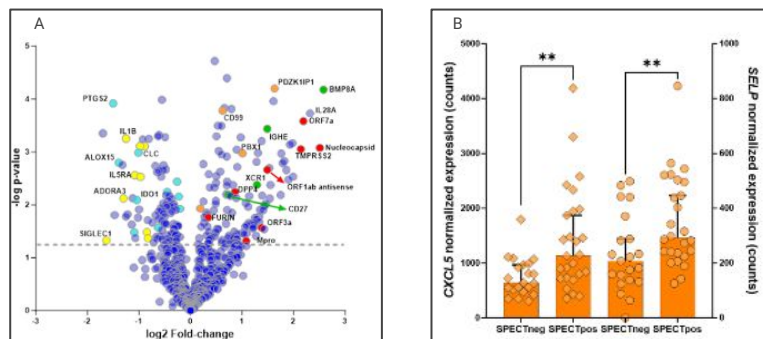
## Results; nuclear imaging

SPECT-CT shows vascular perfusion defects damage. On 53 SPECT-CT ordered, 45 (84%) cerebral blood flow defects identified. (1 confirmed by 18FDG PET scan, 5 18FDG PET scans negative.)



SPECT (Single Photon Emission Computed Tomography using 99mTc-ethyl cysteinate dimer) taken 31 months after acute COVID-19 from a 47-year old male Long COVID patient with abnormal fatigue, disturbed sleep, burning sensations in the legs, loss of words, loss of immediate memory, nausea, difficulty concentrating, claustrophobia, increased pain, shortness of breath, and recurring headaches (clinician-reported severity Duke Severity of Illness (DUSOI) scale 4 out of 5, patient-reported severity COOP chart 24 out of 30). Decreased brain perfusion (blue to green) shown as compared to a database of age- and sex-matched controls, image and protocol courtesy of Dr. Bouazza, Vesalius Hospital, ISPPC, Belgium.

## Results; transcriptomics



A Volcano plot of differentially expressed genes in whole blood samples between Long COVID patients (n=48) and controls (n=12) matched for age, sex, vaccine status, time since acute COVID-19 and comorbidities). Digital transcriptomics (nCounter, Nanostring Technologies Ltd.) was used. Genes highlighted in red correspond to viral RNAs. Genes highlighted in green and salmon correspond to memory B-cell and platelet transcripts, respectively.

B Significant increase (Mann-Whitney test, \*\*p<0.01) of platelet transcripts CXCL5 and SELP (encoding P-Selectin) in Long COVID patients with severe neurocognitive defects and decreased brain perfusion (SPECT pos, n=27), as compared to patients without severe neurocognitive defects (SPECT neg, n=21).

A cerebral perfusion disorder revealed through SPECT-CT serves as a valuable model for emphasizing vascular endothelitis and elucidating symptoms such as cognitive impairment, memory deficits, and other neurological issues. In the initial cohort of 48 patients, a robust statistical correlation was observed between the flow disorder and transcriptomic findings, indicating the presence of viral RNA and platelet activation genes among others. This finding further strengthens the hypothesis of Chronic Covid.

Additional research is underway in the fields of proteomics, platelet biology and cellular neurobiology.

