High serum levels of IL-8 are associated with excessive fatigue in female carriers of X-linked Chronic Granulomatous Disease

Alexander Martin, Newcastle University, 120052895, a.j.martin@newcastle.ac.uk  J.R. Tarn⁴, A. Battersby³, W.F. Ng⁵, C. Cale⁹, D. Goldblatt⁶, A.R. Gennery⁴

1. Introduction
- Chronic Granulomatous Disease (CGD) is a rare disorder of white blood cells leading to serious infection and inflammation.
- 70% of cases are due to an X-linked (XL) mutation.
- There is increasing evidence that female carriers of XL-CGD experience a range of inflammatory symptoms.[1]
- Many XL-CGD carriers also report excessive fatigue[2] which may be due to inflammatory processes mediated by cytokines.
- To date, there has been no investigation of the possible mechanism of this fatigue in XL-CGD carriers.

2. Aim
- To investigate whether XL carriers of CGD have raised serum levels of inflammatory cytokines which are associated with fatigue.

3. Methods
- **Design:** Serum from 52 XL-CGD carriers was compared with inflammatory disease control groups of 10 high and 10 low fatigue Sjogren’s disease patients and 15 healthy controls.
- **Data collection:** Cytometric Bead Array (CBA) immunoassay assessed levels of IL-1α, IL-5, IL-8, IL-10, IL-17, IFNα and IFN-γ using BD Biosciences LSRFortessa™ cell analyser (Figure 1).
- **Data analysis:** FACSDiva, BD Biosciences; FCAP Array, Soft Flow Inc.; SPSS, IBM (Mann-Whitney U Tests).

4. Results
- 25/52 (48%) of XL-CGD carriers reported fatigue on a validated questionnaire[3]
- IL-8 concentration (mean 1459u/ml) was significantly higher in XL-CGD carriers than in healthy controls (mean 72u/ml) (p=0.015) and Sjogren’s disease controls (mean 203u/ml) (p=0.031) as a whole (high and low fatigue grouped).
- IL-8 concentration was significantly higher in the subgroup of XL-CGD carriers who reported fatigue (mean 2405u/ml) than in those who did not (mean 400u/ml) (p=0.005).
- Other investigated cytokines were not significantly raised.

5. Conclusions
- Serum IL-8 is significantly higher in XL-CGD carriers than in healthy and Sjogren’s disease control groups.
- Higher serum IL-8 levels are significantly correlated with higher levels of fatigue in XL-CGD carriers.
- IL-8, which has been associated with fatigue,[4] may be a driver of fatigue in this group via an inflammatory process.
- It is hoped that this initial finding will stimulate further research into how IL-8 influences fatigue in XL-CGD carriers and how its effects can be managed to improve the quality of life for these women.

6. Citations & Acknowledgements
- [3] Multidimensional Fatigue Symptom Inventory Short Form (MFSI-SF)
- This research was supported by a scholarship grant from the Faculty of Medical Sciences, Newcastle University and The Bubble Foundation.
- a. Institute of Cellular Medicine, Newcastle University. b. Clinical Immunology, Great Ormond Street Hospital, London. c. Institute of Child Health, University College London, London.