Investigating UK Biobank blood metrics variation to inform cell therapy manufacturing process control [poster]

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Research Aims
To investigate whether UK Biobank blood metric data shows variation in White Blood Cell count that can act as a healthy population benchmark for Stem Cell Therapy manufacturing process control

Cell therapies are becoming increasingly viable on a clinical basis, to the extent where upscale to centralised or distributed manufacture is possible. Manufacturing processes and control paradigms have been traditionally predicated on minimal variation of the product and the capability to control the manufacturing process using product limits. Automation within traditional manufacture that has adhered to this philosophy has led to rigorous, statistical process controls. While there is a requirement to translate and scale up the production of cell therapies, the manufacturing processes need to understand and accommodate the issues associated with, and context of, using cells as products.

Conventional manufacturing process control would normally be defined as typically 10% to 30% of the defined process limits i.e. less than 0.1 orders of magnitude. Existing work has already defined significant variation of starting materials in Haematopoetic Stem Cell (HSC) therapy exemplars [1, 2, 3] that may be 3 to 6 orders of magnitude variation. But there is now a need to examine a baseline healthy population for variation in blood metrics to further inform potential manufacturing process control paradigms.

Analysis Methodology
UK Biobank [4] was petitioned for access to 502,664 patient records (Table 1). Access to blood metrics and associated data tags were obtained, with emphasis on; age, health state, gender, weight, centre location. These were prioritised to align with existing analyses completed on multi site and single site clinical centre data [1, 2, 3].

At the point that this investigation was carried out, UK Biobank did not directly measure cell markers that specifically identified stem cells such as HSCs. CD34+ cell counts would have been appropriate to directly compare the relatively healthy population of the UK Biobank to the relatively unwell populations in multi and single centre clinical analysis [1, 2, 3]. UK Biobank does however record red blood cell counts, WBC counts and the specific subsets of WBCs such as leukocytes and monocytes. Biological variation was therefore explored as a function of WBCs rather than and as a surrogate to HSCs.

The comma-separated variation output was processed in IBM’s SPSS 22.0 statistics package. Distributions of cell metrics were analysed for normality. The minimum, maximum and range data were defined along with Standard Deviation and Variance. These biological measurements were found to be non-parametric and consequently non-parametric statistical tools were used to compare median and distribution of the data. The Pearson product-moment correlation co-efficient was used to measure linear correlation. Independent samples median tests, independent Mann-Whitney tests (for two independent groups, such as gender) and independent sample correlation co-efficient was used to measure linear correlation. Independent samples median tests, independent Mann-Whitney tests (for two independent groups, such as gender) and independent sample correlation co-efficient was used to measure linear correlation.