Addendum: Systems vaccinology of the BNT162b2 mRNA vaccine in humans

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Since the publication of our original article, we have been alerted to a discrepancy between the expression of sex-specific genes in the cellular indexing of transcriptomes and epitopes by sequencing (CITE-seq) and bulk transcriptomics datasets and the reported gender of the subjects, whose transcriptomes were analysed in these datasets.

CITE-seq: The reported gender of the six participants included in the CITE-seq analysis was correct. However, there was a cross-contamination of the day-1 samples obtained from participants 2049 (male) and 2051 (female), which resulted in the erroneous appearance of cell clusters containing cells of both male and female origin in the CITE-seq data. By analysing single-nucleotide variants, we correctly reassigned the contaminating cells to the appropriate subjects and reanalysed the CITE-seq data. This reanalysis resulted in 242,202 high-quality transcriptomes, as opposed to 242,479 transcriptomes reported previously and resulted in minor changes to Fig. 4c and i and Extended Fig. 10f, but did not affect any of the conclusions.

Bulk transcriptomics: We also discovered that an inadvertent mislabelling of samples had occurred at the genomics core facility during the processing of samples for bulk transcriptomics. Based on the original lab records, we have now reassigned the correct samples to the appropriate subjects and time points. We independently confirmed our reassignment using single-nucleotide polymorphism analysis of banked PBMC samples from each corresponding subject. The correct reassignment resulted in changes to several figures (Figs. 3 and 5 and Extended Data Figs. 1a, 8, 11, and 12) and Supplementary Table 1. The major conclusions from the analysis of bulk transcriptional data, including the dynamics and nature of the transcriptional response, and the transcriptional correlates of T cell and antibody response remain unaffected. Furthermore, the central observation of an enhanced innate transcriptional signature following secondary vaccination was strengthened (Fig. 3) and has now been confirmed by independent studies[1,2]. However, the reassignment of samples to the appropriate time points resulted in more negatively enriched gene sets on day 7 and later, and a diminution of the correlation between the monocyte-associated transcriptional signature and the cross-neutralization potential against the B.1.351 strain (Extended Data Fig. 12). The negatively enriched modules represent innate pathways whose magnitudes at these time points (i.e., days 7, 21, and 28) were negligible relative to their magnitude at day 22 (peak of the response). As such, we do not make strong biological conclusions based on this negligible expression of the innate immunity modules on days 7, 21, and 28. The revised figures and description of the results are incorporated in the online version of the paper.

1. On page 411, in the section "Transcriptional signatures of vaccination," "31 participants" now reads "32 participants", "Six of 185" is now "Four of 185", and "fourfold" is now "twelvefold" in the first three sentences of the paragraph.
2. On page 413, in the section "Comparison with other vaccines," the third sentence now begins with "The responses at day 1 after the prime and boost doses of BNT162b2 were broadly similar", instead of the original "Although the day-1 response to the first dose of BNT162b2 showed little overlap with that of other vaccines, the response at day 1 after the boost was broadly similar". Furthermore, in the sentence beginning, "Meanwhile, day-7 responses", which carries over to page 414, the sentence now ends with "but cell-cycle-related transcriptional modules after both doses were shared with many vaccines", rather than the original "with cell-cycle-related transcriptional modules after the prime dose being the signature shared with many vaccines".
3. On page 415, in the fifth sentence of the section "Transcriptional correlates of adaptive immunity," "monocyte and inflammatory modules were highly associated" has been replaced with "a monocyte module was associated".

The corrected and the published version of the figures and the details of the sample assignment are presented in Supplementary Figs. 1–7 and Supplementary Tables 1 and 2, respectively, for transparency.

Supplementary information is available in the online version of this Amendment.

1. Yamaguchi, Y. et al. Consecutive BNT162b2 mRNA vaccination induces short-term epigenetic memory in innate immune cells. *JCI Insight* **7**, e163347 (2022).
2. Rinchai, D. et al. High-temporal resolution profiling reveals distinct immune trajectories following the first and second doses of COVID-19 mRNA vaccines. *Sci. Adv.* **8**, eabp9961 (2022).