

Supplementary Figure 1: Sample contrast matrix illustrating all of the intra- and inter-patient sample comparisons. The gray cells on the diagonal represent each of the samples where the numbers are the patient IDs, and the letters A and B are for the 1st and 2nd collected semen samples, respectively. The green cells represent the 12 intra-patient comparisons where the 1st and 2nd samples from each patient are compared (12 comparisons). The blue cells represent all the inter-patient comparisons performed (264 comparisons). The epigenetic differences were calculated for each comparison group (i.e. intra- and inter-) across the different genomic regions.

Supplementary Figure 2: Hierarchical clustering of the β -values for the top 600 most leukocyte discriminating probes ([Jaffe, Reinius et al. 2012](#)) with the corresponding β -values from the collected semen samples. The sperm DNA methylation signatures are distinct from those of the FACS-sorted peripheral blood cell populations; neutrophils (granulocytes [Gran]), lymphocytes (CD8+ [CD8T] and CD4+ [CD4T] T cells, CD56+ natural killer cells [NK] and CD19+ B cells [Bcell]) and CD14+ monocytes (Mono).

Supplementary Figure 3: Euclidian distance profiles of the intra- and inter-patient $|\Delta M$ -values| across the genomic regions.

Supplementary Table 1: Pairwise Pearson correlation analysis of intra- and inter-patient sperm methylation levels (M-values).

Supplementary Table 2 : List of 305 significant 5'—C—phosphate—G—3' (CpGs) with greater methylation variability in the inter-patient comparison with respect to the intra-patient comparison. The Wilcoxon test was performed using the mean beta-values for each probe across the patient groups followed by a Benjamin-Hochberg multiple correction. Gene annotation for the CpGs are provided if available. $q < 0.05$ and mean inter- and intra-patient beta-value difference > 0.02 .