

Supplementary Figure 1. Flowchart of experimental design, library construction, and analyses.

All heterozygous SNPs
found in embryo2



Select only phased heterozygous SNPs
and heterozygous SNPs found outside
of LFR contigs



Remove any variant that is not found at a called reference
position in both parents



Remove any variant that is detected in the paternal
grandparents



Remove any variant that is found in a database of 400
healthy octagenarians, 54 unrelated individuals or dbSNP



Remove all variants called in embryo #2 for embryo #1
biopsies and embryo #1 biopsy 1 for embryo #2 as a
heterozygous or homozygous SNP by CGI's standard
pipeline, any variant that is phased, or any variant with
reads found in 1 or more wells. For unphased variants a
well ratio of less than 3.5 X difference between variant
and reference wells and less than 4 wells with co-
existing variant and reference reads was applied.

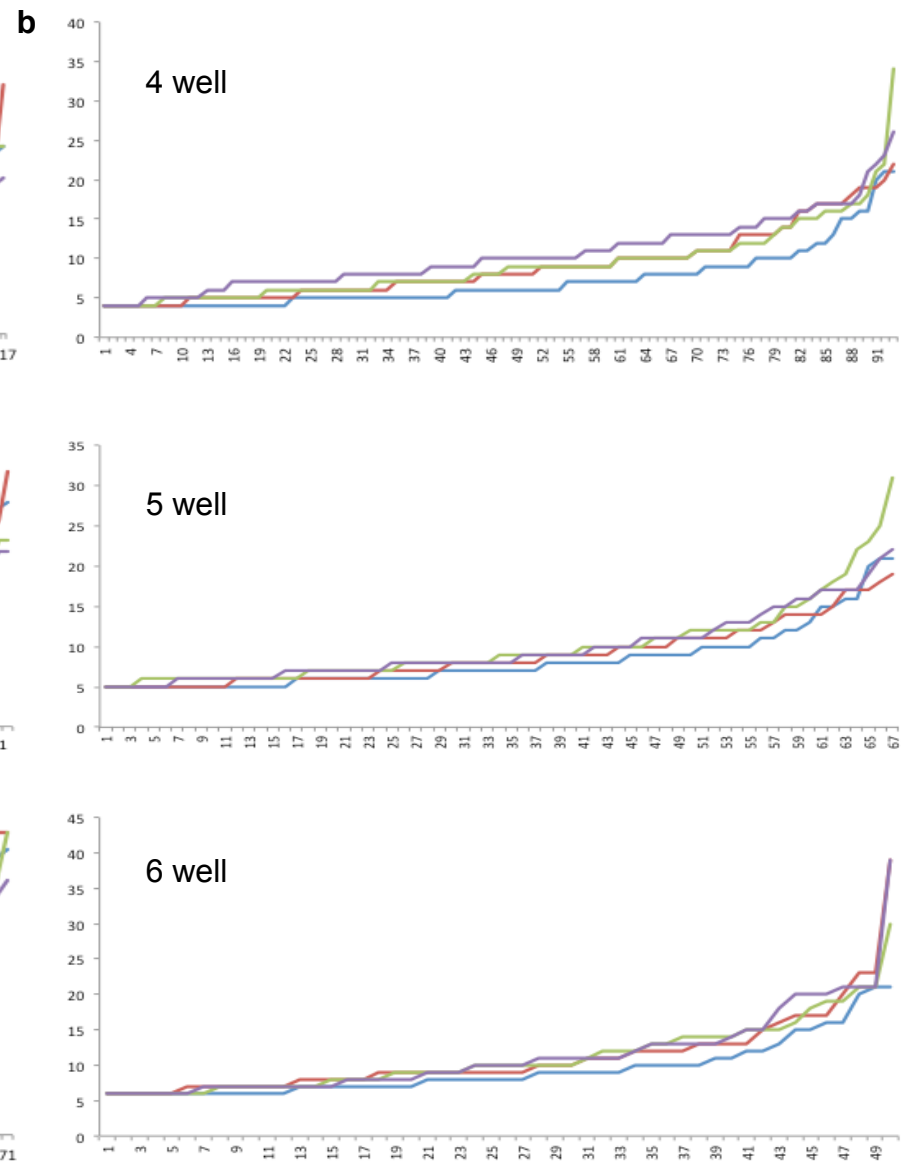
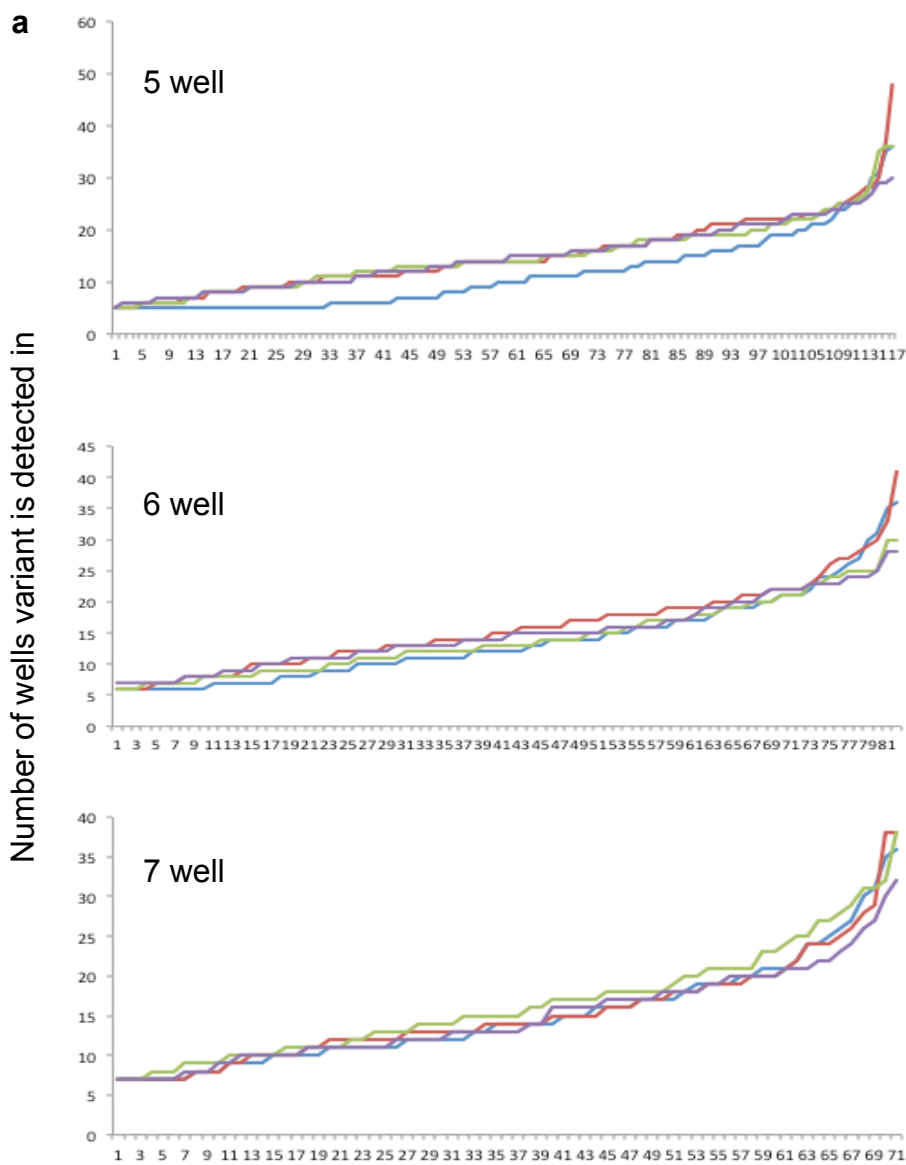


Remove all variants found in 6 or fewer wells



de novo SNVs

Supplementary Figure 2. Analysis flow chart. This series of steps was taken to remove false positive and inherited SNVs. After these filters are applied the large majority of SNVs are *de novo*. There is still the possibility of some false positives (<10) and possibly a few inherited SNVs that are a result of false negative calls in the parents.



Supplementary Figure 3. *De novo* detection and false positive removal well threshold analysis. Different well thresholds were analyzed to determine which wells resulted in *de novo* like SNVs sharing similar properties to 3 random groups of inherited variants. Number of wells a variant was found in was plotted for each variant after first applying the well threshold and then sorting variants based on the number of variant wells for a, embryo #1 biopsy 1, and b, embryo #2. *De novo* variants are plotted in blue, all other colors are randomly selected inherited variants. A well threshold of 6 was used for additional analyses.