

Closing the gaps in the human genome

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Sequence gaps in human chromosome 15 have been closed by the application of 454 technology. Researchers writing in BioMed Central's open access journal *Genome Biology* have described a simple and scalable method for finishing non-structural gaps in genome assemblies.

Manuel Garber worked with a team of researchers from the Broad Institute of MIT and Harvard, Massachusetts, USA, to develop an approach for closing class III gaps, those non-structural gaps that are refractory to clone-based approaches, using 454 sequencing. He said, "While clone-based methods remain an effective means of attacking structural gaps, they will not resolve gaps that arise from sequences recalcitrant to bacterial cloning. The human [genome](#) still contains 127 class III gaps, many of which are likely to be closable by the method described here".

A key difference between the 454 methodology and traditional sequencing is that the 454 process has no bacterial cloning step. Garber and his colleagues designed six primer pairs anchored in unique sequences that tiled the three gaps and used PCR to amplify these regions. They then sheared and directly sequenced the gap-spanning PCR products, using the 454 Life Sciences GS FLX. For each gap, the 454 reads were successfully assembled into a single, high-quality contig spanning the gap region.

Garber said, "The technique we present could be also be applied to the targeted closure of gaps in other finished or near finished genomes such as mouse and dog, which contain 103 and 47 class III gaps, respectively".

More information: Closing gaps in the [human genome](#) using sequencing by synthesis; Manuel Garber, Michael C Zody, Harindra M Arachchi, Aaron Berlin, Sante Gnerre, Lisa M Green, Niall Lennon and Chad Nusbaum; *Genome Biology* 'in press', genomebiology.com/

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