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# Replication landscape of the human genome

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## Summary

Despite intense investigation, human replication origins and termini remain elusive. Existing data have shown strong discrepancies. Here we sequenced highly purified Okazaki fragments from two cell types and, for the first time, quantitated replication fork directionality and delineated initiation and termination zones genome-wide. Replication initiates stochastically,primarily within non-transcribed, broad (up to 150 kb) zones that often abut transcribed genes, and terminates dispersively between them. Replication fork progression is significantly co-oriented with the transcription. Initiation and termination zones are frequently contiguous, sometimes separated by regions of unidirectional replication. Initiation zones are enriched in open chromatin and enhancer marks, even when not flanked by genes, and often border 'topologically associating domains' (TADs). Initiation zones are enriched in origin recognition complex (ORC)-binding sites and better align to origins previously mapped using bubble-trap than lambda-exonuclease. This novel panorama of replication reveals how chromatin and transcription modulate the initiation process to create cell-type-specific replication programs.



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