

## The Draft Genome of Hop (*Humulus lupulus*), an Essence for Brewing

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The female flower of hop (*Humulus lupulus* var. *lupulus*) is an essential ingredient that gives characteristic aroma, bitterness, and durability/stability to beer. However, the molecular genetic basis for identifying DNA markers in hop for breeding and to study its domestication has been poorly established. Here, we provide draft genomes for two hop cultivars (cv. Saazer [SZ] and cv. Shinshu Wase [SW]) and a Japanese wild hop (*H. lupulus* var. *cordifolius*; also known as Karahanasou [KR]). Sequencing and *de novo* assembly of genomic DNA from heterozygous SW plants generated scaffolds with a total size of 2.05 gigabases (Gb), corresponding to approximately 80% of the estimated genome size of hop (2.57 Gb). The scaffolds contained 41,228 putative protein-encoding genes. The genome sequences for SZ and KR were constructed by aligning their short sequence reads to the SW reference genome and then replacing the nucleotides at SNP sites. *De novo* RNA sequencing (RNA-Seq) analysis of SW revealed the developmental regulation of genes involved in specialized metabolic processes that impact taste and flavor in beer. Application of a novel bioinformatics tool, phylogenetic comparative RNA-Seq (PCP-Seq), which is based on read depth of genomic DNAs and RNAs, enabled the identification of genes related to the biosynthesis of aromas and flavors that are enriched in SW. Our results not only suggest the significance of historical human selection process for enhancing aroma and bitterness biosyntheses in hop cultivars, but also serve as crucial information for breeding varieties with high quality and yield.