

Whole-genome sequencing of bulls in key beef and dairy breeds

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Prof. Ruedi Fries and Dr. Hubert Pausch monitor sequence data of breeding cattle. Credit: U. Benz / TUM

An international collaboration known as the '1000 Bull Genomes Project' aims to accelerate breeding for desired traits in beef and dairy cattle while also improving animal health and welfare. Results of the project's first phase—based on sequencing the whole genomes of 234 individual bulls whose direct descendants number in the tens of



millions—are reported in the journal *Nature Genetics*.

According to the researchers, breeding programs could use this information to reduce or eliminate hereditary diseases and to improve the efficiency of milk and beef production.

The bulls whose genomes have been sequenced and analyzed represent four of the most commercially important cattle breeds. Scientists from the Technische Universität München (TUM) contributed data on 43 sires of the Fleckvieh breed, which has spread to every continent from its origin in the Bavarian Alps. The estimated worldwide population of Fleckvieh dairy cows is 40 million. From the widely distributed Holstein-Friesian population, the collaborators obtained whole-genome sequences for 129 bulls with more than six million daughters on dairy farms. The Jersey breed was represented by data from 15 bulls. Previously published genome sequences for 47 Angus cattle were also integrated into the analysis.

Modern breeding practices, together with advances in genome sequencing technology and bioinformatics, have made better prediction of inherited traits not only attainable but also cost-effective on the basis of a relatively small number of individuals. Selection of sires in cattle breeding is intense, and widespread use of artificial insemination means it's not unusual for a hundred thousand animals to be descendants of a single bull. With the ancestors' sequences, breeders now have a leverage tool in hand that allows them to extrapolate the sequence information to the numerous descendants using readily available chip-based DNA microarrays.

Personal Genomics for the Animal Farm

From whole-genome sequencing of the selected bulls – with a total of 28.3 million variants identified – the researchers began building a



database of genotypes. This in turn enables sequence-based genome-wide association studies as well as genomic prediction. As a result, mutations that have a negative impact on <u>animal health</u>, welfare, and productivity can be rapidly identified.

Already in the first phase of the 1000 bull genome project, the researchers see evidence that this approach could help dairy and beef farmers to meet an increasing demand for their products. They tested the usefulness of the database by flagging recessive mutations associated with embryonic death and a lethal skeletal disorder. In addition, genomewide association studies identified variants associated with specific phenotypes, such as high fat content in milk and the curly coat inherited by some Fleckvieh cattle.

In the 10,000 years of cattle breeding, this really is something new. "Whole-genome sequencing of founder animals on this scale is unprecedented for a livestock species," says Prof. Ruedi Fries, Chair of Animal Breeding at TUM. "Our results provide the basis for individualized cattle genetics, one might say 'personal genomics' for cows."

Around the world, consumer demand for beef and dairy products is changing but not diminishing. In a drive to meet <u>cattle</u> breeders' future needs, the 1000 bull genome project has enlisted scientists from Australia, Canada, Denmark, France, Germany, the Netherlands, and the United States.

More information: "Whole-genome sequencing of 234 bulls facilitates mapping of monogenic and complex traits in cattle." Hans D Daetwyler, Aurelien Capitan, Hubert Pausch, Paul Stothard, Rianne van Binsbergen, Rasmus F Broendum, Xiaoping Liao, Anis Djari, Sabrina C Rodriguez, Cecile Grohs, Diane Esquerre, Olivier Bouchez, Marie-Hoelle Rossignol, Christophe Klopp, Dominique Rocha, Sebastien Fritz,



Andre Eggen, Phil J Bowman, David Coote, Amanda J Chamberlain, Charlotte Anderson, Curt P VanTassell, Ina Hulsegge, Mike E Goddard, Bernt Guldbrandtsen, Mogens S Lund, Roel F Veerkamp, Didier A Boichard, Ruedi Fries, and Ben J Hayes. *Nature Genetics*, 13 July, 2014. DOI: 10.1038/ng.3034

This work is based on an earlier publication by TUM and the Helmholtz Zentrum München: "Assessment of the genomic variation in a cattle population by re-sequencing of key animals at low to medium coverage", *BMC Genomics*. 2013 Jul 4;14:446. DOI: 10.1186/1471-2164-14-446

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