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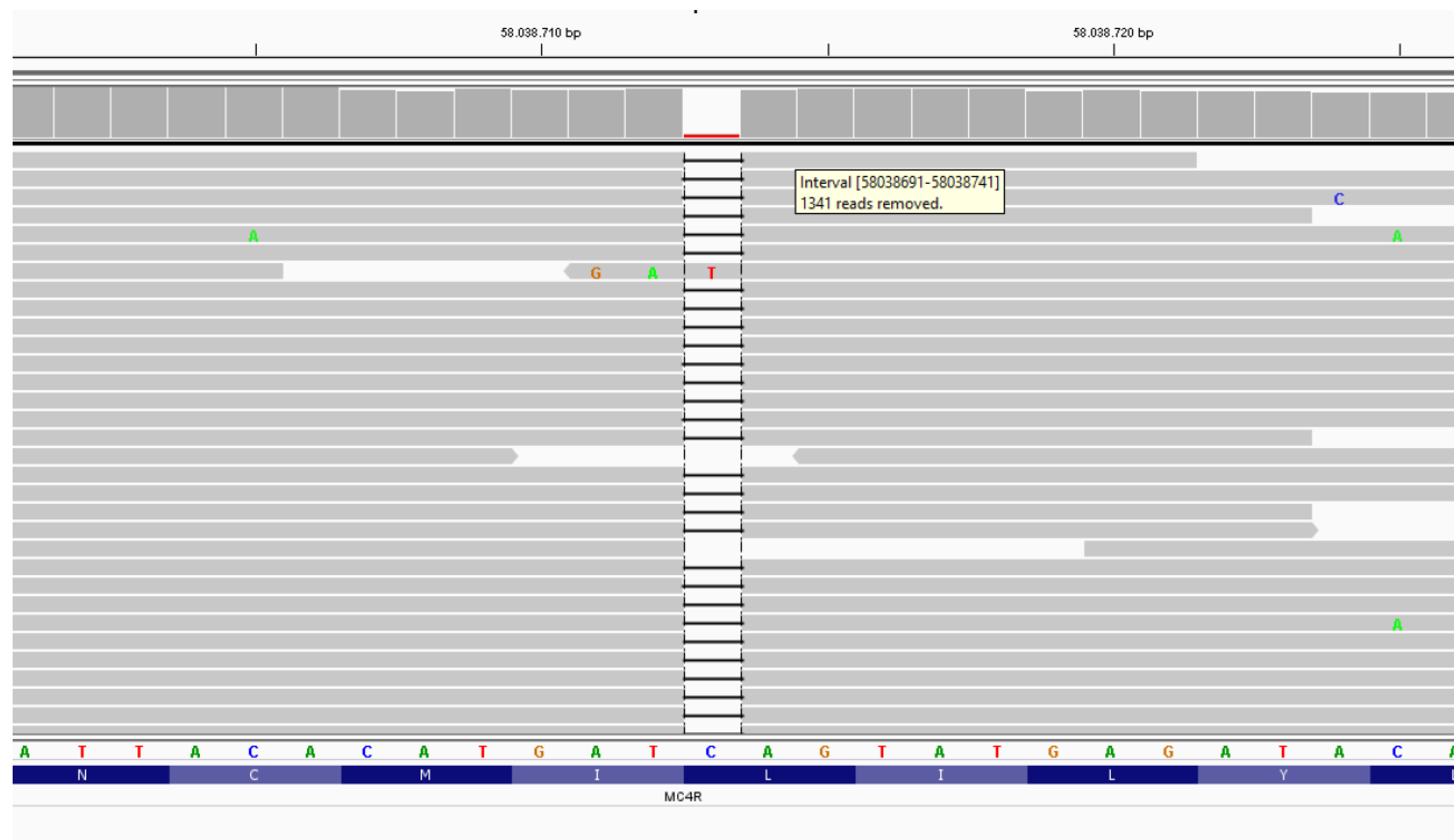
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Conflict of interest: None

The melanocortin-4-receptor gene (MC4R) is a key regulator of energy homeostasis, food intake and body weight which has intensively been analyzed in molecular genetic obesity research. MC4R dysfunction in humans causes hyperphagia, impaired satiety and obesity. Most patients are heterozygotes, with some reports of homozygotes and compound heterozygotes.

## Case:

2 years old boy with progressive weight gain from infancy admitted to the hospital with hyperphagia and increased linear growth. His parents was nonconsanguineous and his birth weight was 3650 gr (0,50 SD). His height and BMI SDS was -1,86; 7,3 SD respectively. There was no phenotype of morbid obesity in the parents or sibling. In his laboratory analyses lipids, fasting glucose and insulin levels were normal. Coding region of the MC4R gene was sequenced by Illumina MiSeq Next Generation Sequencing System.



A novel c.870delG (p.I291SfsX10) homozygous mutation in MC4R gene was detected.

By in-silico analysis softwares this novel mutation predicted to be disease causing and it is expected to have a 32 aminoacids shorter MC4R protein. Mother was shown to be a heterozygous carrier for the mutation.

**Conclusion:** This rare homozygous mutation in MC4R gene markedly impairs its function and is associated with early-onset obesity and hyperphagia. Investigating the mutations in MC4R gene in patients with severe childhood-onset obesity is useful for better patient management and is also important to detect the other family members with same condition. Preimplantation genetic diagnosis might be offered to the families who have mutations in MC4R gene in order to have healthy offsprings.