Common Variants in CYP2R1 and GC Genes Predict Vitamin D Concentrations in Healthy Danish Children and Adults - DTU Orbit (21/01/2019)

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Environmental factors such as diet, intake of vitamin D supplements and exposure to sunlight are known to influence serum vitamin D concentrations. Genetic epidemiology of vitamin D is in its infancy and a better understanding on how genetic variation influences vitamin D concentration is needed. We aimed to analyse previously reported vitamin D-related polymorphisms in relation to serum 25(OH)D concentrations in 201 healthy Danish families with dependent children in late summer in Denmark. Serum 25(OH)D concentrations and a total of 25 SNPs in GC, VDR, CYP2R1, CYP24A1, CYP27B1, C10or88 and DHCR7/NADSYN1 genes were analysed in 758 participants. Genotype distributions were in Hardy-Weinberg equilibrium for the adult population for all the studied polymorphisms. Four SNPs in CYP2R1 (rs1562902, rs7116978, rs10741657 and rs10766197) and six SNPs in GC (rs4588, rs842999, rs2282679, rs12512631, rs16846876 and rs17467825) were statistically significantly associated with serum 25(OH)D concentrations in children, adults and all combined. Several of the SNPs were in strong linkage disequilibrium, and the associations were driven by CYP2R1-rs10741657 and rs10766197, and by GC-rs4588 and rs842999. Genetic risk score analysis showed that carriers with no risk alleles of CYP2R1-rs10741657 and rs10766197, and/or GC rs4588 and rs842999 had significantly higher serum 25(OH)D concentrations compared to carriers of all risk alleles. To conclude, our results provide supporting evidence that common polymorphisms in GC and CYP2R1 are associated with serum 25(OH)D concentrations in the Caucasian population and that certain haplotypes may predispose to lower 25(OH)D concentrations in late summer in Denmark.

General information
State: Published
Organisations: National Food Institute, Division of Nutrition, Division of Toxicology and Risk Assessment, Department of Applied Mathematics and Computer Science, Statistics and Data Analysis, Aarhus University, National Research Centre for the Working Environment
Number of pages: 13
Publication date: 2014
Peer-reviewed: Yes

Publication information
Journal: P L o S One
Volume: 9
Issue number: 2
Article number: e89907
ISSN (Print): 1932-6203
Ratings:
BFI (2019): BFI-level 1
Web of Science (2019): Indexed yes
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 3.01 SJR 1.164 SNIP 1.111
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.11 SJR 1.236 SNIP 1.101
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): CiteScore 3.32 SJR 1.427 SNIP 1.136
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): CiteScore 3.54 SJR 1.559 SNIP 1.148
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): CiteScore 3.94 SJR 1.772 SNIP 1.153
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): CiteScore 4.15 SJR 1.982 SNIP 1.156
Web of Science (2012): Impact factor 3.73