# CCNO

This gene encodes a member of the cyclin protein family, and the encoded protein is involved in regulation of the cell cycle. Disruption of this gene is associated with primary ciliary dyskinesia-19. Alternative splicing results in multiple transcript variants. This gene, which has a previous symbol of UNG2, was erroneously identified as a uracil DNA glycosylase in PubMed ID: 2001396. A later publication, PubMed ID: 8419333, identified this gene's product as a cyclin protein family member. The UNG2 symbol is also used as a specific protein isoform name for the UNG gene (GeneID 7374), so confusion exists in the scientific literature and in some databases for these two genes.

Reduced generation of multiple motile cilia (RGMC) is a novel chronic destructive airway disease within the group of mucociliary clearance disorders with only few cases reported. Mutations in two genes, CCNO and MCIDAS, have been identified as a cause of this disease, both leading to a greatly reduced number of cilia and causing impaired mucociliary clearance. This study was designed to identify the prevalence of CCNO mutations in Israel and further delineate the clinical characteristics of RGMC. We analyzed 170 families with mucociliary clearance disorders originating from Israel for mutations in CCNO and identified two novel mutations (c.165delC, p.Gly56Alafs*38; c.638T>C, p.Leu213Pro) and two known mutations in 15 individuals from 10 families (6% prevalence). Pathogenicity of the missense mutation (c.638T>C, p.Leu213Pro) was demonstrated by functional analyses in Xenopus. Combining these 15 patients with the previously reported CCNO case reports revealed rapid deterioration in lung function, an increased prevalence of hydrocephalus (10%) as well as increased female infertility (22%). Consistent with these findings, we demonstrate that CCNO expression is present in murine ependyma and fallopian tubes. CCNO is mutated more frequently than expected from the rare previous clinical case reports, leads to severe clinical manifestations, and should therefore be considered an important differential diagnosis of mucociliary clearance disorders [1].

1)

Amirav I, Wallmeier J, Loges NT, Menchen T, Pennekamp P, Mussaffi H, Abitbul R, Avital A, Bentur L, Dougherty GW, Nael E, Lavie M, Olbrich H, Werner C, Kintner C, Omran H; Israeli PCD Consortium Investigators. Systematic Analysis of CCNO Variants in a Defined Population: Implications for Clinical Phenotype and Differential Diagnosis. Hum Mutat. 2016 Apr;37(4):396-405. doi: 10.1002/humu.22957. Epub 2016 Feb 4. PubMed PMID: 26777464.