

# MAN1B1-CDG

MAN1B1 mutations cause a recessively inherited form of intellectual disability. MAN1B1-CDG is one of the 26 diseases of the protein N-glycosylation.



## What is MAN1B1-CDG?

Rafiq and colleagues were the first to associate MAN1B1 mutations with a syndromic form of intellectual disability<sup>1</sup>. MAN1B1 (MIM:604346) encodes mannosyl-oligosaccharide alpha-1, 2-mannosidase, a Golgi protein involved in the maturation and secretory pathway of N-glycans. Importantly, great clinical variability has been seen among affected siblings.

## What are CDG?

Congenital Disorders of Glycosylation (CDG) are a rapidly growing group of monogenic metabolic diseases, which counts over 130 different types.

## When to suspect MAN1B1-CDG?

MAN1B1-CDG should be considered in the presence of intellectual disability, particularly associated with facial dysmorphism (e.g prominent eyebrows, bulbous nose tip, tent-shaped mouth with thin upper lip, and large ears), truncal obesity and behaviour issues, (present in approx. 50% of all patients, and becoming more evident around/after adolescence and adulthood) namely aggressiveness, altered sexual behaviour and/or overeating.

## Causes

As the wide majority of CDG, MAN1B1-CDG is an autosomal recessive disorder. Reported mutations include nonsense, missense, splice site and deletions<sup>1,2,3,4,5,6</sup>. The p.R334C mutation has been the most commonly found with 10 diagnosed patients so far<sup>1,2,4,5</sup>.

## Diagnosis

Biochemical features, include a type 2 serum transferrin isoelectric focusing pattern. Mass spectrometry analysis of serum transferrin exhibits a build-up of hybrid N-glycans. The diagnosis is confirmed by mutation analysis. Contact us if you wish to connect with a CDG diagnosis laboratory: [sindromeecdg@gmail.com](mailto:sindromeecdg@gmail.com).

## Major signs and symptoms

### Neurologic

Intellectual Disability (Ranging From Mild to Severe) | Global Developmental Disability (Including Delayed Speech and Psychomotor Milestones) | Epilepsy | Ataxia | Hypotonia | Sensory Processing Disorder

### Behaviour

Aggressiveness (Both Verbal and Physical) | Inappropriate Sexual Behaviour | Overeating | Autism | Tics | Anxiety

### Dysmorphism (Variable)

Hypertelorism | Flat Oval Face | Down-Slanting Palpebral Fissure | Low Frontal Hairline | Curved Eyebrows With Lateral Thinning | Prominent | Bulbous Nose Tip | Thin Upper Lip | Tent Shaped Mouth | Large Ears

### Skeletal

Long Thin Fingers | Hypermobility of the Joints | Scoliosis | Pectus Excavatum | Macrocephaly | Dolichocephaly | Clinodactyly

### Other Symptoms / Signs

Skin Laxity | Overweight (Mainly Truncal Obesity) | Asthma | Cardiac Defects | Hyperglycemia | Mild Coagulation Abnormalities | Mild Increase of Serum Transaminases | Inverted Nipples | Strabismus | Syndactyly | Inability to Regulate Body Temperature (1 patient) | Inability to Process Monosaccharides and Disaccharides (1 patient)

## Prevalence

It has been diagnosed in 35 patients from 22 different families worldwide (for 12 patients nationality is unavailable)<sup>2,6</sup>. Additionally, 2 Australian patients have been diagnosed, but not reported in literature.

(9 Pakistani | 6 Turkish | 3 Iranian | 2 Belgian | 2 Portuguese | 1 Emirati)

Rafiq and coworkers suggested that MAN1B1 mutations could be responsible for as much as 1% of all cases of non-syndromic intellectual disability.<sup>1</sup>

## Clinical Management

Scoliosis and pectus excavatum can be surgically corrected<sup>3,4</sup>. Sleep disturbances have been improved with clonidine intake. Inability to regulate body temperature can lead to episodes of overheating, which may be controlled by keeping the patient in a cool environment and increasing liquid intake. Additionally, panadol can help decrease body temperature.

It is highly recommended that MAN1B1-CDG patients are followed by a multi-disciplinary team of health professionals. These patients might benefit from speech, physical, occupational and psychological therapy. Additionally, nutritional advice and follow-up should be given to these patients.

## Prognosis

Motor skills have been reported to improve with age, whereas intellectual disability seems to be stable and non-progressive overtime<sup>5</sup>. Epileptic seizures may only manifest later in childhood (5 – 10 yrs)<sup>1</sup>. Features, such as hypotonia and macrocephaly have also been reported to spontaneously improve<sup>5</sup>. Overweight may lead to rapid bone maturation and premature puberty<sup>3</sup>. Some patients acquire speech and become independent in their daily hygiene (including toilet trained), whilst others remain non-verbal and highly dependent for their daily care.



[www.researchcdg.com](http://www.researchcdg.com)

### References

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