

TCF4 clinical phenotype guidelines:

Core phenotype (need to be met for PP4)

- Global developmental delay
- Intellectual disability
- Behavioral problems (anxiety)
- Hand flapping
- Characteristic Facial Features (become more apparent with age)
- Deeply set eyes with prominent supraorbital ridges
- Mildly up-slanted palpebral fissures
- Broad nasal root, wide nasal ridge, and wide nasal base with enlarged nostrils
- Overhanging or depressed nasal tip, which may be pointed
- Short philtrum
- Thick vermilion of the lower lip, which is often everted
- Widely spaced teeth

Supportive criteria (do not need to be met for PP4, however in the absence of one core phenotype, two or more supportive phenotypes can be used in its place)

- Prominence of the lower face with a well-developed chin, with age the lower face becomes more prominent and facial features may coarsen
- Mildly cupped ears with over folded helices
- In some individuals, wide mouth with downturned corners and exaggerated Cupid's bow or tented vermilion of the upper lip
- Happy, excitable, frequent smiling, laughter
- Episodic periodic breathing

Additional notes: If information is provided such that a phenotype of Pitt Hopkins syndrome is suspected, with specific minimal features used for the diagnosis, then this can be used for PP4 in lieu of the specific clinical features listed.