

Title: Primary Autosomal Recessive Microcephalies and Seckel Syndrome Spectrum Disorders *GeneReview* Supplementary Information - Cytogenetic Testing

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Note: The following information is provided by the authors listed above and has not been reviewed by *GeneReviews* staff.

### Cytogenetic testing

- In persons with biallelic *MCPH1* mutations, premature chromatin condensation (PCC) in the early G2 phase of the cell cycle and delayed decondensation in the early G1 phase [Trimborn et al 2004] result in (1) an increased frequency of prophase-like cells on routine cytogenetic analysis of peripheral blood (compared to normal reference range of  $\leq 2\%$ ) and (2) poor metaphase banding resolution in routine cytogenetic testing [Trimborn et al 2005]. If misregulated chromosome condensation (increased proportion of prophase-like cells and/or poor chromosome banding resolution) is present on routine karyotype, a *MCPH1* mutation is likely (see Table 1)
- Chromosome instability induced *in vitro* with mitomycin C has been reported in five persons with Seckel syndrome of unknown genotype [Bobabilla-Morales et al 2003]. This analysis is not routinely performed by most cytogenetic laboratories.
- One patient later shown to carry a *MCPH1* mutation was reported with spontaneous chromosome breaks and hypersensitivity to clastogens [Tommerup et al 1993, Farooq et al 2010]
- Increased breakage rate at known fragile sites was reported in persons with SCKL1 [Casper et al 2004].
- If conventional cytogenetic studies are performed, evaluation for premature chromatin condensation (PCC) should be specifically requested, as this feature may be overlooked. PCC will not be detected by chromosome microarray analysis (CMA).
- Individuals with SCKL5 due to mutations in *CEP152* may further show premature centromere separation, an increased number of aneuploidy mitoses (reported in 10% of cells), and - in interphase cells - the presence of multiple nuclei and or the presence of micronuclei. These anomalies cannot be detected by CMA.

## References

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