



## Pathological Mutations in tRNA<sup>Leu</sup>(UUR)

One of the most perplexing aspects of mitochondrial genetics is the marked clinical variability associated with mtDNA mutations. This is dramatically demonstrated for the MTTL1 gene where base substitutions at np 3243, 3252, 3271, and 3291 give MELAS, but the np 3243 mutation can also result in maternally inherited diabetes and deafness. The MTTL1 mutations at np 3303 and 3260 result in hypertrophic cardiomyopathy and myopathy, but the former has a pediatric onset while the latter is adult-onset. While alteration of functions embedded within the gene such as the MTTT for the np 3243 mutation and a muscle specific tRNA processing activity for the np 3302 mutation have been proposed as partial explanations for these phenotypic differences, much of the clinical variability remains unexplained. The mitochondrial transcription terminator binding site is indicated by black dots

