

# Activating GNAS1 gene mutations in patients with premature thelarche

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**Objective** To identify GNAS1 gene mutations in girls with exaggerated and/or chronic fluctuating thelarche for at least 1-year duration with no other signs of precocious puberty, skeletal dysplasia, or typical skin lesions of McCune-Albright syndrome. **Study design** We studied the GNAS1 gene mutation by allele-specific polymerase chain reaction and enzymatic digestion in leukocyte DNA in 23 girls previously described. **Results** Fluctuating thelarche was present in 14 girls and exaggerated thelarche was observed in 9. Molecular study revealed that 6 girls had a substitution of arginine by histidine in codon 201 (R201H [+]). Three R201H (+) girls reached their menarche at a mean chronologic age of 10.8 years and 9 of the R201H (-) girls at a mean age of 11 years. **Conclusions** Activating mutations of GNAS1 gene may be observed in some girls with chronic fluctuating and/or exaggerated thelarche, without other classic signs of McCune-Albright syndrome.