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Molecular cloning and polymorphic analysis of canine 21-hydroxylase gene
as a candidate causing growth hormone-responsive dermatosis in Pomeranians

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Growth hormone-responsive dermatosis (GHRD) is predominantly described in Pomeranians, and the cause of this disease is not completely elucidated. It has previously been reported that Pomeranians have adrenal sex hormone abnormalities attributed to the partial defect of 21-hydroxylase (21-OH), which may associate with the pathogenesis of GHRD. The hormonal condition and the characteristic of clinical manifestation of GHRD in Pomeranians are similar to those of non-classical 21-OH deficiency (21-OHD) in humans caused by the mutations of 21-OH gene. To clarify whether the partial 21-OHD reported in Pomeranians is due to similar mutations of its gene to those in humans, I initially cloned and sequenced full length of canine 21-OH gene, then carried out the polymorphic DNA analysis among Pomeranians both affected and unaffected with GHRD and control Beagles. Nucleotide and deduced amino acid sequences of

canine 21-OH were highly homologous with those of other species previously reported. In the several nucleotide differences among the subject dogs for sequencing 21-OH gene, all transitions detected in the coding region were silent. In the 5' flanking region, a monobasic transition found only in Pomeranians was located within the putative steroidogenic factor (SF)-1 binding site which plays a significant role to regulate the expression of 21-OH gene. These results suggest that this transition might interfere with the binding of SF-1 to the promoter region of 21-OH gene and decrease its expression, and thereby cause the adrenal sex hormone abnormalities in Pomeranians. By further investigations, this finding could make contributions to the better understanding on the pathogenesis of human 21-OHD and the selective breeding to eliminate the allele possibly causing canine GHRD.