Investigation into the Inheritance and Biochemistry of Chondrodysplasia in Texel Sheep

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Abstract

A skeletal chondrodysplasia characterized by dwarfism and angular deformity of the forelimbs has been recognized over four seasons in Texel and Texel cross lambs on three related properties. Some affected lambs have normal co-twins indicating that the disease is not dietary, but likely to be the result of a genetic disorder. This study reports on the inheritance and biochemistry of this newly discovered chondrodysplasia in Texel sheep. The outcome of a backcross trial between putative carrier ewes and affected rams provided evidence that indicated that the chondrodysplasia has an autosomal recessive mode of inheritance, and that it is likely to be caused by a single gene defect.
Analysis of proteoglycan constituents of cartilage by SDS-PAGE, followed by sulfate-specific staining indicated that the biochemical abnormality lies in the level of sulfation of proteoglycans in the extracellular matrix of affected animals. It was also shown by SDS-PAGE that there were no differences in the major collagen constituents of cartilage between unaffected and affected animals. A candidate gene, the diastrophic dysplasia sulfate transporter, was determined based on its involvement in the process of sulfation of proteoglycans and its involvement in characterized human dysplasias, which resemble Texel chondrodysplasia both phenotypically and biochemically. PCR amplification and sequencing of 85.4 % of this gene revealed no nucleotide differences between the exonic DNA of normal, carrier, and affected animals. While this reduced the likelihood that this gene is causative in the chondrodysplasia, it does not eliminate it as a candidate, based on the fact that a mutation may exist in the region not sequenced, including the possibility of splice site mutations.

Abbreviations

ACG -1B	Achondrogenesis type 1B
AO2	Atelosteogenesis type 2
APS	Adenosine-phosphosulfate
ATP	Adenosine triphosphate
ATPSK2	Adenosine triphosphate sulfurylase/ Adenosine-phosphosulfate kinase 2 gene
bm	Brachymorphic
BSA	Bovine serum albumin
cDNA	Synthetic DNA, generated from RNA
cmd	Cartilage matrix deficiency
COL1	Collagen 1 protein domain
COL2A1	Collagen type II alpha 1 gene
COL3	Collagen 3 protein domain
COL9A1	Collagen type IX alpha 1 gene
COL9A2	Collagen type IX alpha 2 gene
COL9A3	Collagen type IX alpha 3 gene
COL10A1	Collagen type X alpha 1 gene
COL11A1	Collagen type XI alpha 1 gene
COL11A2	Collagen type XI alpha 2 gene
CSPGs	Chondroitin sulfate proteoglycans
DDSH	Dyssegmental dysplasia, Silverman-Handmaker type
Dmm	Disproportionate micromelia
DNA	Deoxyribose Nucleic Acid
dNTP	Deoxynucleoside triphophate (dATP, dTTP, dCTP, dGTP)
DTDST	Diastrophic dysplasia sulfate transporter
DTT	Dithiothreitol

ECM	Extracellular Matrix
EDTA	Ethylene diamine tetra-acetic acid
FACIT	Fibril- associated with interrupted triple helices
FGFR3	Fibroblast growth factor receptor 3 gene
GAG	Glycosaminoglycan
GCG	Genetics Computer Group
HPLC	High performance liquid chromatography
Hspg2	Heparin sulfate proteoglycan gene 2
MED	Multiple epiphyseal dysplasia
ocd	Osteochondrodysplasia
OSMED	Oto-spondylo-megaepiphyseal dysplasia
PAPS	Phosphoadenosine-phosphosulfate
PCR	Polymerase chain reaction
PMSF	Phenylmethane-sulfonylfluoride
QTL	Quantitative trait loci
SDSC	San Diego supercomputer center
SDS	Sodium dodecyl sulfate
SDS-PAGE	Sodium dodecyl sulfate polyacrylamide gel electrophoresis
SED	Spondyloepiphyseal dysplasia
SEDC	Spondyloepiphyseal dysplasia congenita
SEMD	Spondyloepimetaphyseal dysplasia
SMCD	Schmid metaphyseal chondrodysplasia
SMD	Spondylometaphyseal dysplasia
SJS	Schwartz-Jampel syndrome
SK2	Sulfate kinase 2 gene
TAE	Tris acetate EDTA
TCA	Trichloroacetic acid
TE	Tris –EDTA buffer
UV	Ultra-violet light

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