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CANDIDATE GENE APPROACH IN MOLECULAR ANALYSIS OF ICHTHYOSIS DEFECT IN CHIANINA CATTLE

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Ichthyosis represents a group of disorders of keratinisation affecting humans and animals. It is characterized by an excessive amount of superficial scale on the skin, resembling the scales of a fish. It is quite rare and can be inherited (genetic or congenital) or develop later in life (acquired). The inherited forms of ichthyosis are usually evident at or soon after birth. The scaling of ichthyosis affects most if not all areas of the skin. Several inherited forms have been described in man, but the classification criteria are still not well defined and attempts to correlate them with the animal disorders have lead to inconsistencies in classification and nomenclature, particularly in the bovine conditions. Nevertheless two main forms have been reported in cattle. Foetal ichthyosis is incompatible with life and affected animals are aborted or survive no more than a few days after birth. The skin, usually hairless, is covered by large horny plates separated by deep fissures which correspond to normal cleavage lines of the skin. The tight, inelastic skin causes emersions of mucocutaneous junctions and small ear pinnae are often seen. Ichthyosis foetal has been described in Norwegian Red Poll, Friesian and Brown Swiss calves. The other form, congenital ichthyosis, is the less severe expression of the defect and affected cattle live longer. The lesions are similar to those in the previous form, but are less serious and more localized. It has been reported in Jersey, Pinzgauer, Chianina and Holstein-Friesians. Recently, in Chianina breed cases of ichthyosis have been reported in Italy. Chianina is a valuable autochthonous cattle breed. Among 12 affected calves notified, 6 were investigated; they were sons of the same sire and were born in the same farm in the last year. Autoptic analysis confirmed the diagnosis of ichthyosis and the hypothesis of a genetic cause has been formulated. Pedigree data have been collected from the ANABIC (National Breeder Association Italian Beef Cattle) database and microsatellite genotyping has been performed on the available animals to confirm the parentage. Data confirmed that all the Ichthyosis cases have been related to a single sire widely used in the recent past in Italy. Moreover, the disease showed an authosomal recessive single trait Mendelian inheritance. Karyological analysis and R-banding did not show structural anomalies. Being of great importance to identify any potential carrier in the breed, we chose TGM1 as candidate gene of ichthyosis by comparative analysis with the human disease. TGM1 in man has been mapped on chromosome 14q11 and mutations in this gene reduce the activity of TGase1, a critical enzyme in the cornified cell envelope assembly line. More than 30 different mutations of TGM1 gene have been identified. The alteration occurs when the patient is homozygote for a single mutation or heterozygote for two

different mutations on TGM1 gene. By now the complete cDNA sequence for TGM1 gene is available for man, rat, rabbit and dog. It is missing for the bovine. We aligned bovine ESTs from the NCBI database and the human aa sequence of the gene by TBLAStN (www.ncbi.nlm.nih.gov) to obtain a theoretical sequence of the bovine TGM1. Specific bovine primers were designed on this sequence to amplify the whole cDNA. On a sample of muscle from a Chianina cattle RT and both 5' and 3'RACE have been performed. Sequence analysis of the amplicons allowed to obtain the whole bovine gene. Sequencing of the gene is in progress on bioptic samples from suspected carriers (dams and sires of Ichthyosic newborn calves) as well as on autoptic samples from affected calves to identify causative mutations.