Assignment\(^1\) of N-acetyl-D-glucosaminidase (\textit{Mgea5}) to rat chromosome 1q5 by tyramide fluorescence in situ hybridization (T-FISH): synteny between rat, mouse and human with Insulin Degradation Enzyme (IDE)

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\(^1\) To our knowledge this is the first time this gene has been mapped in rat.

\section*{Rationale and significance}

Many nucleocytoplasmic proteins are reversibly modified by the monosaccharide, N-acetylglucosamine (O-GlcNAc), O-linked to serine or threonine residues (Wells et al., 2001). The on reaction is catalyzed by O-GlcNAc transferase (OGT) and the off reaction by the O-GlcNAc-selective N-acetyl-D-glucosaminidase (O-GlcNAcase) (Dong et al., 1994; Gao et al., 2001; Wells et al., 2002). Because \(\beta\)-cells express very high levels of OGT (Roos et al, 1998; Hanover et al., 1999, 2001) and because GlcNAc synthesis can be driven by the availability of glucose in \(\beta\)-cells, these cells accumulate O-GlcNAc to a greater degree than in other tissues when the glucose concentration is elevated (Liu et al., 2000; Konrad et al., 2000). This O-GlcNAc accumulation in \(\beta\)-cells might make these cells very dependent on the activity of the O-GlcNAcase. Here we report synteny between the rat O-GlcNAcase gene (\textit{Mgea5}) with insulin-degrading enzyme gene (\textit{Ide}) to rat chromosome 1q5.

\section*{Materials and methods}

Tyramide fluorescence in situ hybridization was carried out essentially as described (Van Tine et al., 1998). Cytogenetic quality slides were purchased from SeeDNA (Toronto, Canada).

\textbf{Probe name(s):} O-GlcNACase  \\
\textbf{Probe type:} cDNA  \\
\textbf{Insert size:} Vector: pBS (KS-)  \\
\textbf{Proof of authenticity:} Sequencing  \\
\textbf{Gene reference:} AY039679

\textbf{Probe name(s):} IDE  \\
\textbf{Probe type:} cDNA  \\
\textbf{Insert size:} Vector: pBS (KS-)  \\
\textbf{Proof of authenticity:} Sequence  \\
\textbf{Gene reference:} NP_037291

\section*{Results and discussion}

\textbf{Mapping data for Mgea5}

\textbf{Most precise location:} 1q5  \\
\textbf{Number of cells examined:} 20  \\
\textbf{Number of cells with specific signal:} 1 (0), 2 (0), 3 (5), 4 (15) chromatids per cell  \\
\textbf{Location of background signals (sites with \(\geq 2\) signals):} none observed

The Goto-Kakizaki (GK) rat is a well-characterized model for type 2 diabetes (Galli et al., 1996; Ling et al., 1998). The phenotype of GK exhibits several features typical of the disease, such as fasting hyperglycemia, impaired secretion of insulin in response to glucose, and insulin resistance. Congenic strains have been established by transfer of GK alleles onto the genome of the normoglycemic parental F344 rat through repeated back-crossing of GK with F344 (Fakhrai-Rad et al., 2000; Galli et al., 1999). This genetic analysis of the GK rat revealed several separable loci for these diabetes-associated phenotypes, the major one being \textit{Niddm1}, located at the distal part of chromosome 1. This locus contains the IDE gene and the GK rat has alterations in \textit{Ide} that have been associated with part of the diabetes phenotype (Fakhrai-Rad et al., 2000). Given the proximity of the IDE gene in both human and mouse genomes with MGEA5, the functional data suggesting a role for MGEA5 in diabetes (Roos et al., 1998; Hanover et al., 1999, 2001; Liu et al., 2000; Konrad et al., 2000) and the association of the IDE locus with this form of type 2 diabetes in the rat, we...
determined the relative positions of the IDE and MGEA5 loci in the rat. In humans, the O-GlcNAcase gene (MGEA5) is located at gene map locus 10q24.1 → q24.3 (Heckel et al., 1994), very close to the position of the IDE gene (Epinosa et al., 1999). This region of chromosome 10 also has strong genetic linkage to a susceptibility marker of type 2 diabetes (Duggirala et al., 1999) and Alzheimer’s disease (Bertram et al., 2000; Ertekin-Taner et al., 2000; Myers et al., 2000). The mouse O-GlcNAcase gene (Mgea5), which was identified as the previously cloned hyaluronidase 5 gene (Genbank, AF132214), is located on chromosome 19 and is also close to the mouse IDE gene locus (GenBank, XM_123402). The observation of proximity between the IDE gene and the O-GlcNAcase genes in the mouse and human suggest that these genes may be syntenic and that this synteny also occurs in the rat genome.

References


