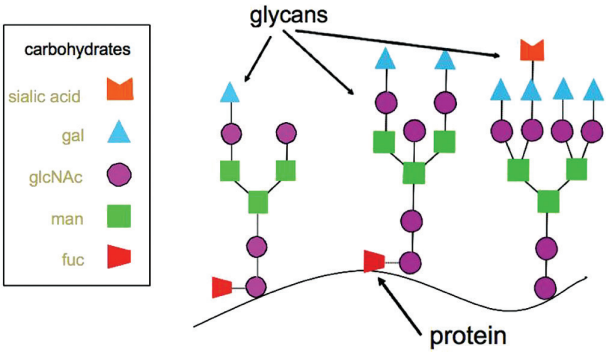

FIGURE 9.12 Schematic drawing of carbohydrate residues (or glycanic structures) present on some protein sequences.

Glycosylation is the most frequent PTM. The terms *glycan* and *polysaccharide* are defined by the International Union of Pure and Applied Chemistry (IUPAC) as synonyms meaning "compounds consisting of a large number of monosaccharides linked glycosidically." However, in practice, the term *glycan* may also be used to refer to the carbohydrate portion of a glycol conjugate, such as a glycoprotein, glycolipid, or a proteoglycan, even if the carbohydrate is only an oligosaccharide. Glycans usually consist solely of O-glycosidic linkages of monosaccharides. For example, cellulose is a glycan (or, to be more specific, a glucan) composed of β-1,4-linked D-glucose, and chitin is a glycan composed of β-1,4-linked *N*-acetyl-D-glucosamine.

Glycans can be homo- or heteropolymers of monosaccharide residues and can be linear or branched. The chemical modifications introduced are very complex owing to the glycan structures that are added to the protein skeleton. Protein glycosylation engages endoplasmic reticulum and Golgi apparatuses. A glycosylation consists of branching on the protein, on determined amino acids (for instance, for *N*-glycosylation, Asn, which is in the Asn-X-Thr sequence), and sugar groups such as mannose, fructose, or galactose, following a well-determined order. These glycosylation chemical reactions will lead to the making of "sugar chains," more or less complex and diversified, considering all the possible attaching combinations (number of antenna(e) on a glycosylation site and the nature of sugars making up this antenna), even if some mandatory sequences are found in each structure.

Finally, the end of the sugar chain is most often capped by a sialic acid in the form of neuraminic *N*-acetyl acid (NANA) in human cells, when for many mammals, a part of the sialic acid is in the form of neuraminic *N*-glycolyl acid (NGNA), because the gene that codes for the enzyme that allows the NANA form to become NGNA is muted and inactive in humans. This species specificity is important when choosing systems involving carbohydrates expression or production of the recombinant protein of interest, to ensure that the sialylation is as close as possible to the human form. The mature protein, so "glycolyzed" and more or less "sialylated," gets some characteristics that are more or less acidic, with a changed isoelectric point (pI). Consequently, at the end of PTMs, the protein appears not as a single entity but as a mix, a molecular population with the same basic protein structure (primary sequence imposed by