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Review

# Spectrins and the Golgi

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**Abstract**

Several isoforms of spectrin membrane skeleton proteins have been localized to the Golgi complex. Golgi-specific membrane skeleton proteins associate with the Golgi as a detergent-resistant cytoskeletal structure that likely undergoes a dynamic assembly process that accommodates Golgi membrane dynamics. This review discusses the potential roles for this molecule in Golgi functions. In particular, it will focus on a recently identified distant cousin to conventional erythroid spectrin variously named Syne-1, Nesprin, myne, Enaptin, MSP-300, and Ank-1. Syne-1 has the novel ability to bind to both the Golgi and the nuclear envelope, a property that raises several intriguing and novel insights into Golgi structure and function. These include (1) the facilitation of interactions between Golgi and transitional ER sites on the nuclear envelope of muscle cells, and (2) an ability to impart localized specificity to the secretory pathway within large multinucleate syncytia such as skeletal muscle fibers.


*Keywords:* Golgi; Spectrin; Syne-1; Transitional ER; COPII; Nuclear envelope; Neuromuscular junction; Syncytium

## 1. Golgi-specific spectrin membrane skeleton proteins

Much of the effort aimed at understanding the role of the cytoskeleton in the organization and function of the Golgi apparatus has focused on the golgin family of coiled-coil proteins [1] and the microtubule cytoskeleton, including microtubule-based motors and centrosomes [2]. However, there is also significant evidence that the actin cytoskeleton plays an important role at the Golgi. Perturbations of the actin cytoskeleton have been shown to give rise to alterations in Golgi structure [3,4], and several actin-binding proteins are known to play some role in Golgi function. These include myosins, both conventional [5] and unconventional [6], and members of the spectrin super-family [7,8]. This review discusses the latter class of molecules, the spectrins.

Spectrins are members of a diverse group of cytoskeletal proteins that share a common structural organization. All spectrins contain multiple copies of a ~106 amino acid repeat that folds into an intra-molecular, triple helical coiled-coil (for review see [9,10]). The sequential arrangement of these spectrin repeats allows for the formation of a freestanding, elongated, rod-shaped molecule. Many spectrins also contain an amino terminal actin-binding site comprised of a pair of calponin homology domains, which are critical for assembly of spectrin into cytoskeletal structures. Spectrins can also possess binding sites for the peripheral membrane protein ankyrin (for review, see [11]), which couples the spectrin cytoskeleton to the cell surface. Spectrins commonly assemble into planar cytoskeletal sheets composed of spectrin molecules cross-linked by short actin filaments that underlay membrane surfaces (Fig. 1a, for review, see [12]). This arrangement forms the basis for the two main functions attributed to the spectrin cytoskeleton: the maintenance of membrane structural integrity and the formation of discrete membrane domains. The Golgi complex, a membranous organelle comprised of various membrane domains arranged in a complex structural organization that is coupled to its function, has a notable requirement for these two functions attributed to the spectrin membrane skeleton.

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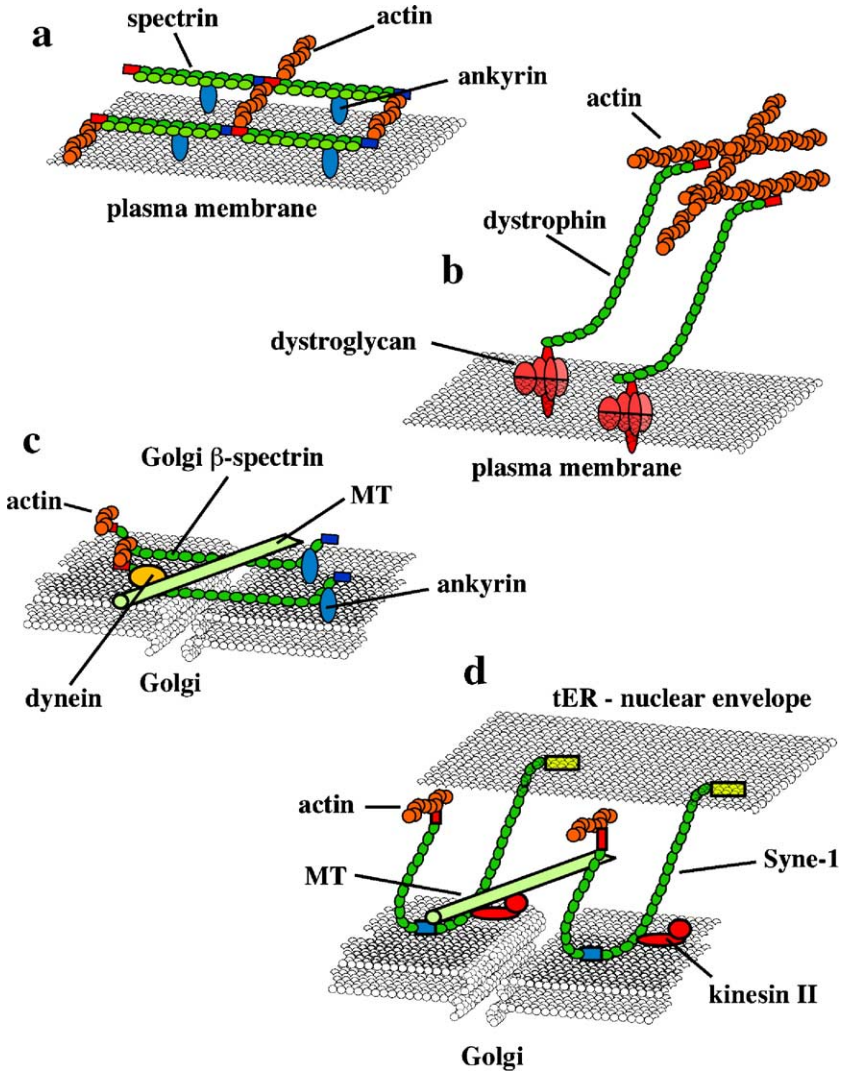


Fig. 1. Spectrins super-family members of the plasma membrane and Golgi. (a) At the plasma membrane, spectrin forms a planar cytoskeletal sheet that underlies the cytoplasmic surface. Spectrin heterodimers (green) are cross-linked by short actin filaments (orange), and the resulting meshwork is linked to the surface by ankyrin. (b) Dystrophin (green) serves as a tether that links dystroglycan complexes (red) of the plasma membrane to the cortical actin cytoskeleton. (c) While the structural organization of the Golgi-specific spectrin membrane skeleton has yet to be elucidated, it seem likely that these "conventional" spectrins would form a planar sheet reminiscent of what is found at the plasma membrane. Golgi-spectrin molecules (green) are thought to interact with dynactin/dynein (yellow), Golgi-specific ankyrin (blue) and probably actin (orange). (d) In muscle cells, Syne-1 (green) could tether the Golgi to tER sites of the nuclear envelope. Syne-1 could also bind nearby actin filaments (orange) via its N-terminal actin binding site and microtubules (MT) through kinesin II (red).

The earliest evidence for a Golgi-specific spectrin came from studies examining the distribution of erythroid spectrin isoforms in non-erythroid cells [7]. An antibody to erythrocyte beta-spectrin was found to prominently stain the Golgi complex in cultured rat kidney cells [7]. Subsequently, a high molecular weight (271 kDa) variant of erythrocyte spectrin was reported to localize to the Golgi complex [8]. Two distinct isoforms of Golgi-specific ankyrins have also been identified. One of these, Ank195, is a 195-kDa Golgi-specific protein that cross-reacts with erythroid ankyrin-specific antibodies [13]. The other, AnkG119, is a truncated form of the major brain ankyrin AnkG [14].

Spectrins are members of a diverse family of proteins called the spectrin super-family. In addition to "conventional spectrins," which include erythroid and non-erythroid spectrin isoforms, the spectrin super family also includes α-actinin, the evolutionary precursor to all spectrins, and the distrophin/utrophin subspecies (for review see [15]). This latter class of molecules resemble conventional spectrins in that they are composed of sequentially arranged spectrin repeats and because they possess amino-terminal actin-binding determinants. However, they differ substantially from spectrin in their primary amino acid sequence. Functionally, all spectrin family members appear to share a common function of linking the plasma membrane to the