Seminars in Cell & Developmental Biology xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Seminars in Cell & Developmental Biology

journal homepage: www.elsevier.com/locate/semcdb

Review

Functional implication of the common evolutionary origin of nuclear pore complex and endomembrane management systems

Ivan Liashkovich*, Victor Shahin*

Institute of Physiology II, University of Münster, Robert-Koch-Set. 27b, 48149 Münster, Germany

ARTICLE INFO

Article history:
Received 24 April 2017
Accepted 26 April 2017
Available online xxx

Keywords:
Nuclear pore complexes
Nucleocytoplasmic transport
Calthrin mediated endocytosis
Coated vesicles
Ran GTPases

ABSTRACT

Nuclear pore complexes (NPCs) are the sole gateway between the cytoplasm and the nucleus serving both as stringent permeability barrier and active transporters between the two compartments of eukaryotic cells. Complete mechanistic understanding of how these two functions are implemented within one and the same transport machine has not been attained to date. Based on several lines of structural evidence, a hypothesis was proposed postulating that NPCs shares common evolutionary origin with other intracellular systems responsible for active management of endomembranes. In this review we attempt to summarize the evidence supporting this hypothesis. The structural data obtained so far is evaluated and supplemented with the analysis of the functional evidence. Based on this analysis, a model is proposed which integrates the knowledge from the field of NPC function with that obtained from other endomembrane management systems in an attempt to shed new light on the mechanism of the NPC active transport.

Contents

1. Introduction to endomembrane management systems: evolutionary perspective

The high complexity and diversity of eukaryotic organisms we observe today may in great part originate from the fact that at some point in the history of life ancestral organisms gained an ability to precisely control the shape of their plasma membrane [1]. As the next step various components of the plasma membrane became completely internalized and formed independent intracellular compartments each offering the possibility of precise control over its content and environment. This compartmentalization enabled the cells to perform functions which were previously incompatible with the rest of the intracellular environment leading toward diversification and increased adaptability. Various components of the endomembrane management systems have subsequently diversified to such an extent that any immediate resemblance of the proteins involved in organizing and modulating endomembranes has become essentially undetectable. Nevertheless, the major players have retained a significant ultrastructural resemblance shared among distinct functional domains of the endomembrane management system. Based on this similarity, a hypothesis was proposed that despite the diversity all components of the endomembrane management system have originated from a common ancestor, which provided an ability to sculpt and maintain curved membranes. This common ancestral coatomer later on evolved into highly specialized, highly divergent systems as we know them today [2]. One such system is represented by the nuclear envelope delimiting the nucleus, a defining feature of eukaryotic

* Corresponding authors.
E-mail address: shahin@uni-muenster.de (V. Shahin).

http://dx.doi.org/10.1016/j.semcdb.2017.04.006
1084-9521/

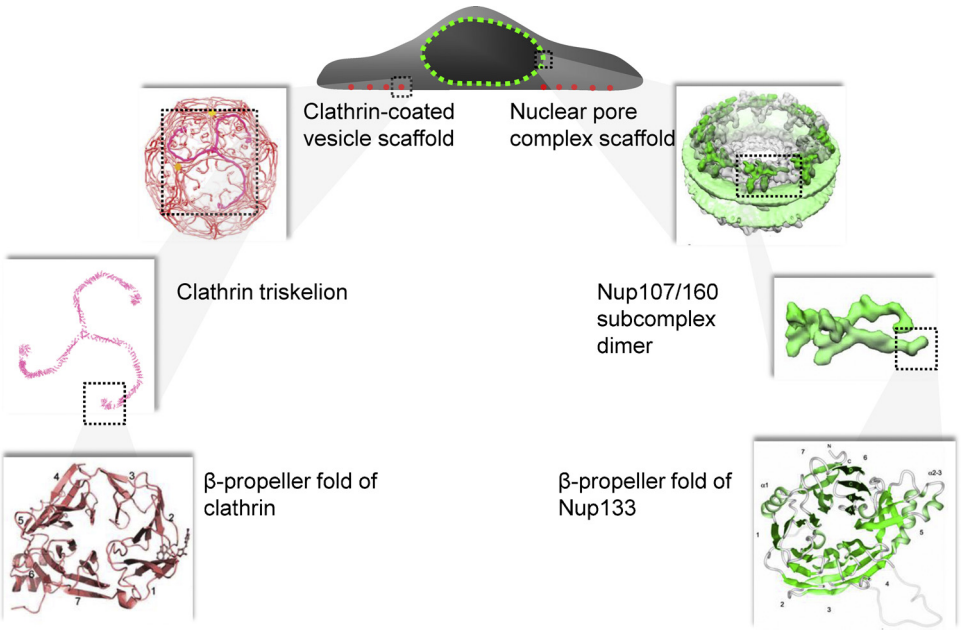

Fig. 1. Common structural themes between clathrin-coated vesicles and nuclear pore complexes (NPCs). Scaffold complexes of clathrin-coated vesicles (left) share a number of structural similarities with the scaffolds of the NPCs. The most prominent is the β-propeller fold shared by several critical components of both systems. Clathrin structures are modified from [6,7]. NPC structures are modified from [8,9].

cells. Separation of the nucleus from the remaining bulk of the cell has provided an additional level of control by decoupling the process of transcription from translation. Nuclear pore complexes (NPCs) which serve as the gateway between the cytoplasm and the nucleus are believed to represent a highly specialized example of the endomembrane coats which has diverged the strongest from the common ancestor. This specialization has resulted in a development of a unique set of NPC functions not all of which are fully understood to date. In this review we will focus on the nuclear envelope and the NPC and its putative relation with the endomembrane management machinery. We will summarize the structural and functional evidence in favor of the common evolutionary origin of these systems and try to extend the parallels between them in an attempt to generate new hypotheses to improve our understanding of the NPC function.

2. Hypothesis of the common origin of membrane coats: structural evidence

The major arguments in favor of the common evolutionary origins of endocytic/NPC originate from structural evidence. The similarity becomes particularly apparent when we compare the overall structure of NPC with an endocytic clathrin-coated pit intermediate prior to scission from the plasma membrane (Fig. 1). Schematic section profiles across a budding clathrin-coated vesicle and an NPC show that the major structural constituents of both are highly curved lipid bilayers and highly structured protein scaffolds which are responsible for maintaining the highly curved membranes [3]. For the purposes of this review we will focus on the structural and functional constituents of the NPC and attempt to correlate their structure/function relationship to putative counterparts from diverse systems involved in the endomembrane management. We would like to stress that no single system presents a fully equivalent functional analog of the NPC. Rather, individual functionalities displayed by various NPC subsystems can be found scattered among widely diverse processes which are found in other systems. Therefore, diverse functional components relevant for the discussion here are pooled together into a broad category of "endomembrane management system components". In most cases, however, the two primary pathways we will be referring to are the clathrin mediated endocytosis [4] and the COPII system of protein transport from the rough endoplasmic reticulum to the Golgi [5].

The major structural components of the NPC involved in maintaining the highly curved membranes comprise two outer ring complexes which sandwich the inner ring complex containing the bulk of the machinery responsible for NPC function [10]. The key structural building block of the outer rings is the Y-shaped Nup107/160 subcomplex. The overall structural organization of the Nup107/160 subcomplex is to some degree reminiscent of the key component of clathrin coat, the clathrin triskelion (Fig. 1). However, when we consider how individual subcomplexes are arranged in both cases, the similarity becomes less evident. While the endocytic coat is composed of polymerized clathrin triskelia forming nearly perfect hexagonal lattice [11,12], the scaffold of the NPC demonstrates circular arrangement of Nup107/160 subcomplex [8,10]. As we go one level deeper into the structural organization of individual proteins and their domains the similarities become very prominent once again. In fact, computationally predicted domain organization of scaffold nucleoporins served as one of the first indications of the evolutionary relationship and possible common ancestry of the membrane coats involved in sculpting the lipid bilayers in both endocytic and nuclear envelope membranes [13].

As our knowledge on 3D organization of the membrane coat proteins progressed further the hypothesis of common evolutionary origin was substantiated by the emerging crystal structures of individual nucleoporins [14–16]. It was confirmed that despite the multitude of individual polypeptide subunits [17,18] required for building a functional NPC scaffold many of them share the structural themes common among all components of the intracellular membrane management systems [19]. If we consider the heavy chain of clathrin as a prototype membrane coat unit and compare its domain and fold structure [20] to those found in scaffold proteins of the NPC [8] it becomes apparent that the α-solenoid

Please cite this article in press as: I. Liashkovich, V. Shahin, Functional implication of the common evolutionary origin of nuclear pore complex and endomembrane management systems, Semin Cell Dev Biol (2017), http://dx.doi.org/10.1016/j.semcdb.2017.04.006