




Review

# Preserving Genome Integrity: Unveiling the Roles of ESCRT Machinery

Mattia La Torre <sup>1</sup>, Romina Burla <sup>1,2</sup> and Isabella Saggio <sup>1,\*</sup>

<sup>1</sup> Department of Biology and Biotechnologies “Charles Darwin”, Sapienza University, 00185 Rome, Italy; mattia.latorre@uniroma1.it (M.L.T.); romina.burla@uniroma1.it (R.B.)

<sup>2</sup> CNR Institute of Molecular Biology and Pathology, 00185 Rome, Italy

\* Correspondence: isabella.saggio@uniroma1.it

**Abstract:** The endosomal sorting complex required for transport (ESCRT) machinery is composed of an articulated architecture of proteins that assemble at multiple cellular sites. The ESCRT machinery is involved in pathways that are pivotal for the physiology of the cell, including vesicle transport, cell division, and membrane repair. The subunits of the ESCRT I complex are mainly responsible for anchoring the machinery to the action site. The ESCRT II subunits function to bridge and recruit the ESCRT III subunits. The latter are responsible for finalizing operations that, independently of the action site, involve the repair and fusion of membrane edges. In this review, we report on the data related to the activity of the ESCRT machinery at two sites: the nuclear membrane and the midbody and the bridge linking cells in the final stages of cytokinesis. In these contexts, the machinery plays a significant role for the protection of genome integrity by contributing to the control of the abscission checkpoint and to nuclear envelope reorganization and correlated resilience. Consistently, several studies show how the dysfunction of the ESCRT machinery causes genome damage and is a codriver of pathologies, such as laminopathies and cancer.

**Keywords:** ESCRT; cell division; nuclear envelope sealing; midbody; genome integrity



**Citation:** La Torre, M.; Burla, R.; Saggio, I. Preserving Genome Integrity: Unveiling the Roles of ESCRT Machinery. *Cells* **2024**, *13*, 1307. <https://doi.org/10.3390/cells13151307>

Academic Editor: Francois-Michel Boisvert

Received: 10 July 2024

Revised: 2 August 2024

Accepted: 2 August 2024

Published: 5 August 2024



**Copyright:** © 2024 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

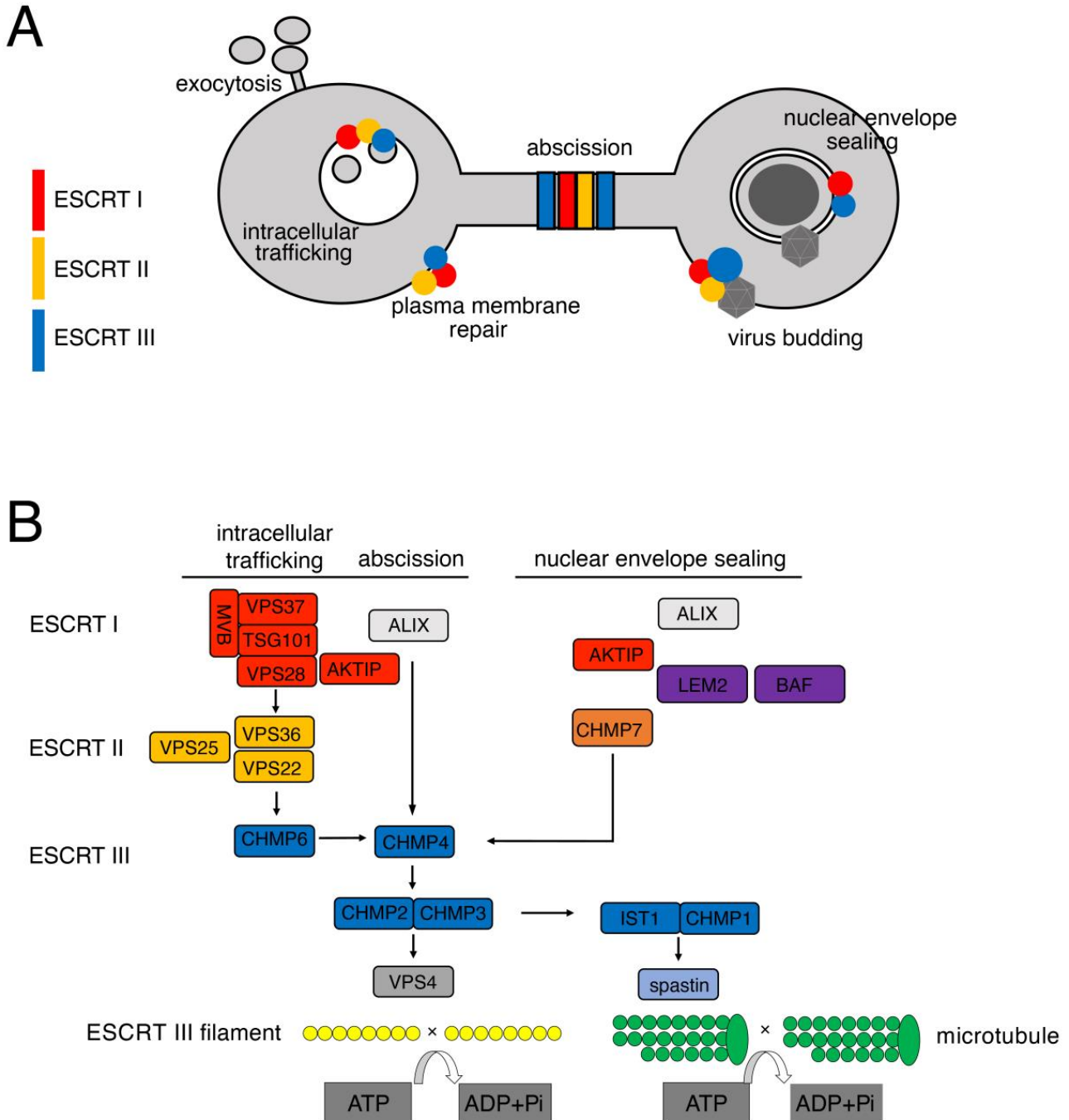
## 1. The ESCRT Machinery

### 1.1. The ESCRT Subunits

The endosomal sorting complex required for transport (ESCRT) is a machinery composed of protein complexes that contribute to multiple cellular processes, such as cytokinesis [1], endosome maturation [2], neuronal pruning [3,4], the nuclear envelope [5,6], and plasma membrane repair [7–9]. In addition, the ESCRT machinery has been implicated in viral replication and budding [10–13] (Figure 1A). The complexes or groups of the machinery are the ESCRT 0, ESCRT I, ESCRT II, and ESCRT III (Figure 1B). By parallel mechanisms, operated at different sites, the ESCRT 0 and ESCRT I subunits initiate the process mediated by the ESCRT machinery and recruit the ESCRT II complex. The ESCRT II subunits help in the recruitment and assembly of the ESCRT III complex. Eventually, the ESCRT III subunits mediate inverse membrane involution finalizing membrane scission or sealing [14–18].

The definition and functional characterization of the different components of the ESCRT machinery were first assessed in yeast and successively paralleled in mammals and other organisms (Table 1). Yeast ESCRT subunits include the ESCRT 0 Vps27, corresponding to HRS-HGS in mammals [19,20]; the ESCRT I Vps23, Vps28, Vps37, and Mvb12 corresponding to, respectively, VPS23 or TSG101 [21], VPS28 [22], VPS37a, b, c, d [23,24], and MVB12a, b in mammals [15,25]; the ESCRT II Vps36, Vps22, and Vps25 corresponding to mammalian EAP45, EAP30, and EAP20, respectively [17,18,26–28]; and the ESCRT III Vps2, Vps24, Snf7, and Vps20, corresponding to mammalian CHMP2A, B, CHMP3, CHMP4A, B, C, and CHMP6, respectively [18,29–33]. CHMP7, which works on nuclear envelope sealing in mammals, has been described as a hybrid ESCRT II/III subunit [32,34–36]. In addition to

the ESCRT subunits, several accessory proteins contribute to the activity of the machinery. These include Bro1, in yeast, corresponding to ALIX in mammals [37], and IST1 that works in concert with the ESCRT III complex and possesses structural similarities to the ESCRT III CHMP3 [38]. All the ESCRT components, except the ESCRT III subunits, bind cargo and/or other ESCRT components. The ESCRT III subunits serve to complete the pathway operated by the machinery and for its disassembly, which happens via the activity of the AAA + ATPase VPS4 complex [18,33,39].



**Figure 1.** Cellular processes involving the ESCRT machinery. **(A)** Schematic representation of the functions of the ESCRT machinery. ESCRT I (red); ESCRT II (yellow); ESCRT III (blue), virus symbol (dark grey). **(B)** Schematic representation of the cascade of ESCRT complexes recruited at the site of action. ESCRT I (red); ESCRT II (yellow); ESCRT III (blue).

**Table 1.** ESCRT components in yeast, flies, and mammals.

Complex Name	Yeast ( <i>S. cerevisiae</i> )	Flies ( <i>D. melanogaster</i> )	Mammals
ESCRT 0	Vps27 [40] Hse1 [40]	Hrs [41] dmel/stam [42]	HRS-HGS [20] STAM1, 2 [43]
ESCRT 1	Vps23 [44] Vps28 [44]  Vps37 [44]  Mvb12 [44]	erupted/tsg101 [45] dvps28 [46,47]  vps37A *, vps37B [48]  mvb12 [49]	TSG101 [21] VPS28 [22] VPS37a [23] VPS37b [23] VPS37c [24] VPS37d [23] MVB12a [15,25] MVB12b [15,25]
ESCRT II	Vps36 [17] Vps25 [17] Vps22 [17]	vps36 [50,51] vps25 [47,52] larsen/vps22 [50,53]	EAP45 (VPS36) [26–28] EAP20 (VPS25) [26] EAP30 (VPS22) [26]
ESCRT II/III	Chm7 [54,55]	CG5498 *	CHMP7 [34–36]
ESCRT III and associated proteins	Vps2 [29] Vps24 [29]  Snf7 [29]  Vps20 [29] Ist1 [59] Vps60 [29] Did2 [29]	vps2 [56] vps24 [47]  shrub [47,57]  vps20 [58] ist1 [60,61] chmp5 [60,61] chmp1 [61]	CHMP2A [29] CHMP2B [29] CHMP3 [29] CHMP4A [30] CHMP4B [30] CHMP4C [30] CHMP6 [31] IST1 [38] CHMP5 [61] CHMP1A [62,63] CHMP1B [62,63]
VPS4-ATPase complex	Vps4 [64] Vta1 [66]	vps4 [3,65] vta1 * [67]	VPS4A [32,33] VPS4B [32,33] LIP5 (VTA1) [68]
BRO1 proteins	Bro1 [69]	ALiX (CG12876) [60,70]	ALIX (PDCD6IP) [37]

\* predicted ortholog (Flybase).

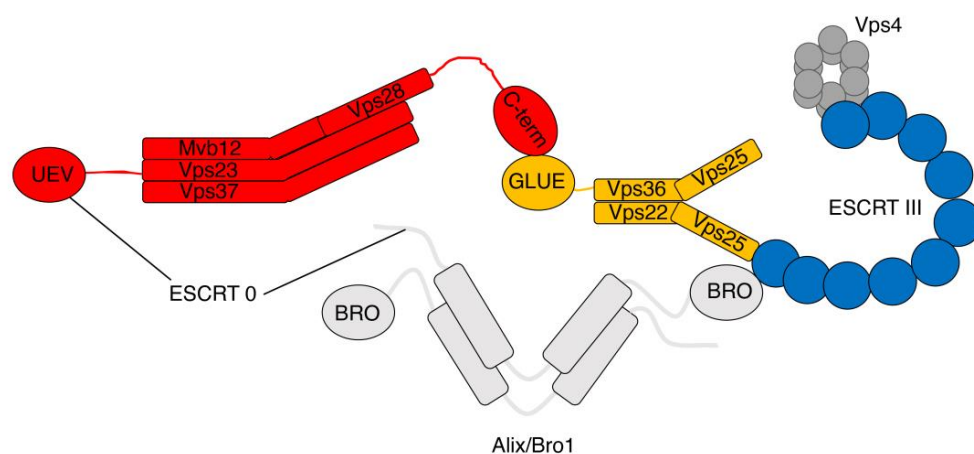
The comprehension of the full picture of the structure–function organization of the ESCRT subunits and of their site of action is in continuous evolution and expansion, along with the identification of new ESCRT-associated factors. AKTIP, for example, is a recently discovered ESCRT I associated protein. The database annotation of AKTIP points to human TSG101 as the AKTIP top-hit homologue with high probability. AKTIP, as the ESCRT I VPS23/TSG101, includes the ubiquitin E2 variant domain and interacts with the ESCRT I VPS28 [71]. Differently from TSG101, AKTIP does not include a proline-rich domain required for the interaction with CEP55 [1,71]. AKTIP is detected in the nucleus and in the cytoplasm and is enriched in distinct foci at the nuclear rim [72–75]. AKTIP has been associated with HOOKs, a group of proteins impinging on vesicle trafficking, and with ESCRT components in cytokinesis [71,76]. During cytokinesis, AKTIP is recruited at the midbody together with the ESCRT subunits.

### 1.2. Structural Organization of the ESCRT Subunits

In support of its pivotal function in the biology of the cell, the ESCRT machinery has ancient origins. In fact, many archaeal species possess ESCRT proteins, and the machinery is conserved during evolution. Metagenome analyses show that Asgard archaea, for example, possess components of the ESCRT I, ESCRT II, and ESCRT III complexes, and, as in mammals, ESCRT III subunits execute the final stages of membrane processing [77–79]. Multiple studies of reverse genetics highlight the presence of ESCRT I, ESCRT II, and ESCRT III genes in *Drosophila melanogaster* [46,47,80]. Recent evidence describes new functions for *Drosophila* ESCRT subunits, such as that of the ESCRT III component Shrub that maintains the septate junction and guarantees epithelial tissue integrity in larvae [81].

Structural studies have shed light on the ESCRT protein domains that are involved in the assembly of the different complexes (Figure 2). In the ESCRT I complex, the core is

made of helical hairpins from the three components: Vps23, Vps28, and Vps37 [16]. This core tethers the ubiquitin E2-variant domain of Vps23 to the ESCRT I C-terminal domain of Vps28 [44,82]. According to the original structural model [19], ESCRT II subunits contain tandem repeats of winged-helix domains and are recruited by ESCRT I via the so-called GLUE of the ESCRT II Vps36 [17,83]. ESCRT III subunits do not form stable complexes, and attempts to perform structural studies were slowed by this aspect. However, the crystal structure of human VPS24, CHMP3, was revealed showing that it includes five helices with a core of a hairpin formed by two of the helices [38,84].



**Figure 2.** Structure of the ESCRT complexes. Schematic representation of the structural organization of the ESCRT complexes. The UEV domain of Vps23 is responsible for the interaction with ESCRT 0 components (black line), whereas the C-terminal domain of Vps28 interacts with the GLUE domain of Vps36. The Y shaped ESCRT II complex is responsible for the recruitment of ESCRT III subunits. Vps4 is recruited by ESCRT III subunits. ESCRT I (red); ESCRT II (yellow); ESCRT III (blue).

In the following paragraphs, we review the data concerning the role of the different subunits of the ESCRT machinery in controlling the integrity of the nuclear envelope on the one side and the process of abscission on the other. In both cases, we analyze how the machinery impacts the integrity of the genome.

## 2. The ESCRT Machinery and Genome Integrity at the Nuclear Envelope

### 2.1. The Organization of the Interphase Nuclear Envelope

In eukaryotic cells, the genome is separated from the nucleoplasm by the nuclear envelope. This is composed of the outer nuclear membrane in continuation with the endoplasmic reticulum and by the inner nuclear membrane juxtaposed to the lamina. This latter element is a meshwork composed mainly of lamin type A and B [85–88]. Lamins type A are encoded by the LMNA gene and have two isoforms, A and C, produced by alternative splicing events. B-type lamins are encoded by the LMNB1 and LMNB2 genes, respectively. Most metazoans express B-type lamins in support of a critical and conserved role of the lamina in the organization of the nuclear organelle. B-type lamins are essential and expressed during development; A-type lamins are present only in differentiated cells. B-type lamins are mostly detected at the nuclear envelope. A-type lamins are detected also in the nucleoplasm serving in multiple roles, including the control of chromatin organization and function [89–91]. The nuclear envelope is interrupted by the nuclear pore complexes to which lamins provide support. Super-resolution microscopy analyses have shown that the nuclear pore complex component TPR is a determinant in the association of the nuclear pore complex to lamin C [92–94].

The lamina is also the resident site for a plethora of proteins. Smoyer et al. identified more than 400 inner nuclear membrane proteins [95]. Among these, there is the LAP2-Emerin-Man1 (LEM)-domain protein subgroup that includes MAN1 [96], LEM2 [97], the lamina-associated polypeptide 2 (LAP2) [98], and emerin [99–101]. Other well characterized

proteins involved in the integrity and function of the nuclear envelope are the SUN-domain proteins, SUN1 [102] and SUN2 [103,104], and the lamin B receptor [105–107]. In addition, the inner nuclear membrane is in contact with the cytoplasm via the LINC (Linkers of the nucleoskeleton to the cytoskeleton) protein complexes [108,109]. LINC factors associate with the lamina or with lamin associated proteins and traverse the outer nuclear membrane to reach at the cytoplasmic side [110,111].

The nuclear envelope, the lamina, and the lamin-interacting proteins contribute to the spatial distribution of chromatin. Chromatin structural compartmentalization was first described by Carl Rabl and Theodor Boveri and refined by the seminal works of Cremer et al. [112] and Cremer et al. [113]. More recent studies have given the molecular details of the spatial architecture of the genome inside the nucleus based mostly on the usage of chromatin conformation capture, 3C techniques [114,115]. Integrating the seminal studies defining the compartmentalization of chromosomes in discrete territories with 3C-technique based data allowed the identification of chromatin topologically associating domains (TADs) [116]. TADs are genomic stretches stabilized by the presence of transcription factors and cohesins [117,118]. 3C techniques have also been useful to define the presence and molecular characteristics of genomic stretches interacting with lamins, the lamin associating domains (LADs) [119–121]. Immunofluorescence and biochemical analyses have, in addition, shown how the nuclear envelope associates with the chromatin via the LEM domain proteins [101,122,123]. MAN1 and emerin bridge with the chromatin via another factor named BAF [124–126]. The lamin B receptor contacts chromatin through HP1 [127–129].

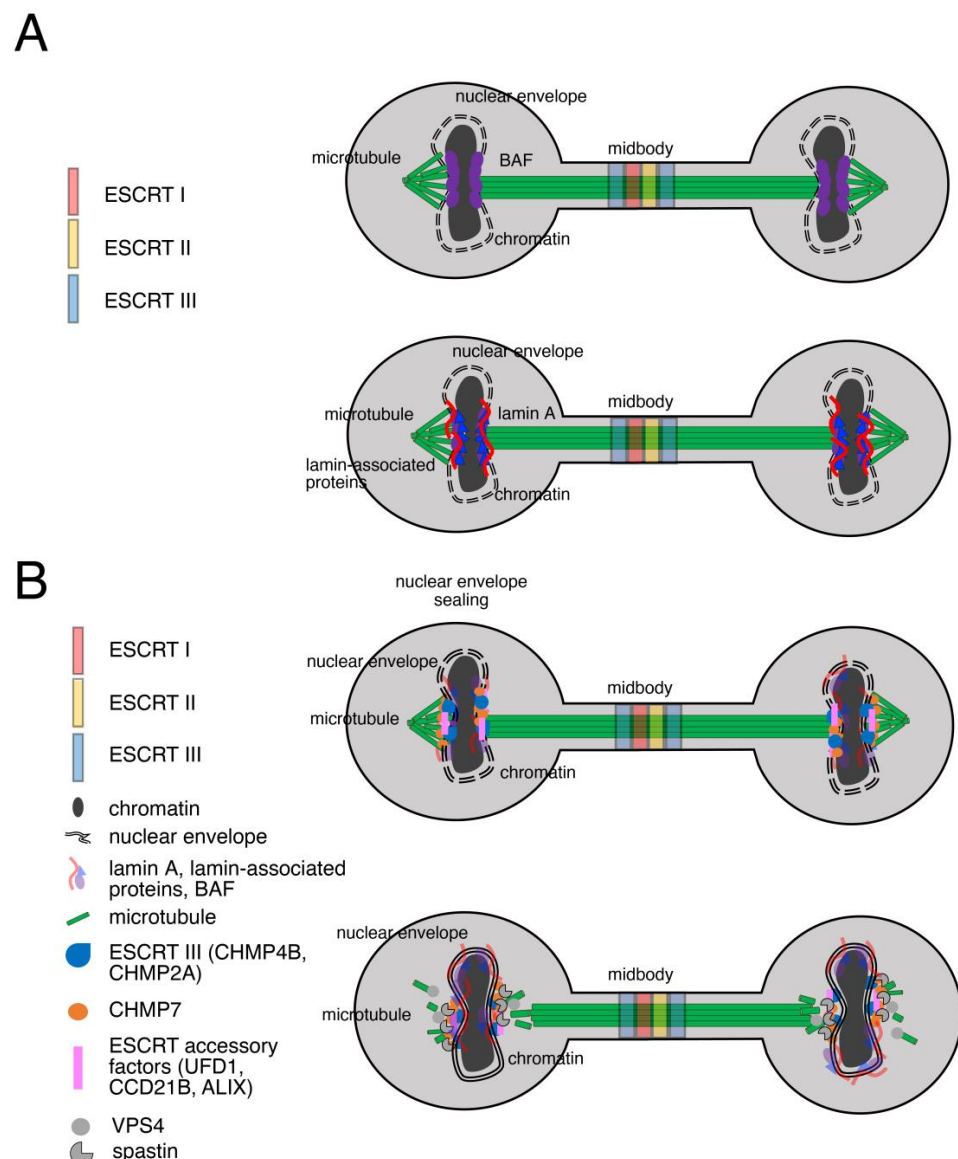
## 2.2. The Dynamics of the Nuclear Envelope and Role of ESCRTs

The process of cell division exhibits variations across different organisms and cell types. In metazoans and higher eukaryotes, open mitosis is prevalent. This type of mitosis is characterized by the fragmentation of the nuclear envelope. In contrast, lower eukaryotes like *S. cerevisiae* and *S. pombe* commonly undergo closed mitosis, where the nuclear envelope remains intact [130,131]. Notably, exceptions exist, as seen in *Cryptococcus neoformans* and certain strains of *Ustilago*, which display a unique form of open mitosis. Some higher eukaryotes engage in semi-open mitosis, where the rearrangements of the nuclear envelope are minimal [132–134].

In open mitosis, the breakdown of the nuclear envelope requires a series of intricate events leading to the temporary disassembly of the nuclear envelope that then has to be followed by its reformation [135]. This is a carefully regulated process initiated during prophase [136]. Several molecular mechanisms contribute to this event. Notably, the phosphorylation-mediated disassembly of the nuclear pore complex marks a critical step. Kinases such as CDK1, NEK, and PLK1 phosphorylate nucleoporins, leading to nuclear pore complex disintegration [136]. Concurrently, lamins undergo phosphorylation by kinases like CDK1/cyclin B, initiating their depolymerization and favoring subsequent events in nuclear envelope breakdown [135,137,138]. Spindle microtubule-generated forces contribute to nuclear envelope retraction, creating tension that results in the stretching and tearing of the nuclear envelope, ultimately leading to its fragmentation [139,140]. Dynein is needed for attaching spindle microtubules to the nuclear envelope, creating pulling forces towards the centrosome [141–144]. The endoplasmic reticulum undergoes significant remodeling during G2/M transition, further contributing to the completion of nuclear envelope breakdown [145–147]. Finally, the orchestration of nuclear envelope breakdown involves the phosphorylation of nuclear envelope-associated proteins, which disrupts protein–protein interactions and triggers the dissociation of these components contributing to the overall structural rearrangement of the nuclear envelope [148–153]. The retraction of the nuclear envelope facilitated by mitotic spindle microtubules involves the withdrawal of the nuclear envelope from chromatin, which is an actively regulated process [133,154,155]. Studies in different organisms, including fission yeast, demonstrate the active regulation of chromatin detachment through post-translational modifications and the involvement of the protein complex Lem2-Nur1 [156,157].



Following nuclear envelope breakdown, when mitosis is not yet completed, the nucleus starts to reorganize its architecture for the next interphase. Here, a set of proteins is recruited progressively around the chromatin, constituting the so-called core region (Figure 3A). BAF is first detected at the chromatin, followed by multiple lamin-associated proteins, as LEM2 and LAP2alpha, followed by emerin, LAP2beta, and MAN1 along with lamin A [158–161]. During telophase, the organization of the two daughter rims around chromatin is visible along with the midbody region between the nascent cells. In mammalian cells, telomeres have a defined dynamic in the anaphase to telophase stage, during which they are enriched at the nuclear envelope through interactions between SUN1 and the telomeric protein RAP1. This distribution of telomeres is presumed to contribute to chromatin domain reorganization including the juxtaposition of heterochromatin at the nuclear lamina [162,163].



**Figure 3.** ESCRT recruitment and function at the nuclear envelope. (A) Schematic representation of the recruitment of the core proteins at the chromatin at the end of mitosis. ESCRT I (red); ESCRT II (yellow); ESCRT III (blue); BAF (purple); chromatin (dark grey); microtubule (green); lamin A (red curved line); lamin-associated proteins (blue triangle); nuclear envelope (black double dotted line). (B) Schematic representation of the recruitment of the ESCRT subunits during nuclear envelope sealing. ESCRT I (red); ESCRT II (yellow); ESCRT III (blue).

To complete the compartmentalization of the genome at the end of the mitotic process, the nuclear envelope discontinuities, due also to the presence of residual microtubules traversing the nascent rim, are repaired by the ESCRT machinery (Figure 3B). The subunits involved in this process are the ESCRT III CHMP4B and CHMP2A and the specialized nuclear ESCRT II/III hybrid factor CHMP7, along with the ESCRT accessory factors UFD1, CCD21B, and ALIX [5,6,36,164–167]. VPS4 and spastin complete the process of nuclear envelope sealing by regulating the disassembly of the complexes, acting, respectively, on the ESCRT III and on microtubules [5,157,168].

An interesting link has been established between CHMP7 and LEM2, which relates as well to the spatiotemporal interpretation of the nuclear reassembly process. Namely, liquid–liquid phase separation has been suggested for the assembly of LEM2 and CHMP7 around residual spindle microtubule bundles, in connection with the chromatin-binding factor BAF [35,167,169–172]. LEM2 is thus reputed to be a transmembrane ESCRT adaptor protein, and this vision highlights that the nuclear reassembly dynamic phase involves chromatin, chromatin-binding factors, lamin-binding factors, the ESCRT machinery, and, eventually, lamin [35,169].

The activity of the ESCRT III in repairing nuclear envelope discontinuities is required also during the interphase. Indeed, nuclear rim ruptures occur in the interphase during cell migration in confined space, upon mechanical stress, in cancer metastases or consequent to genetic mutations [173–176]. These nuclear ruptures are repaired via the concerted action of BAF, LEM2, and ESCRT III. Specifically, cytoplasmic BAF localizes onto DNA at nuclear ruptures, contributing to the recruitment of LEM2 and CHMP7 [177].

### 2.3. Nuclear ESCRT Genome Integrity

The massive process of nuclear reorganization, happening in the final phases of mitosis, calls for an interdependence between the correct reorganization of chromatin in the daughter cells and the activity of the ESCRT machinery. Chromothripsis has been associated with nuclear envelope composition defects and defective nuclear pore complex assembly, impacting genome integrity and function [178]. In analogy, in micronuclei, a defective rim composition has been related with the control of ESCRT III recruitment and function. Indeed, although the ESCRT III subunit CHMP7 is correctly recruited at the micronuclear rim, its spatiotemporal distribution is not correctly restricted [179]. This dysfunctionality is a driver of membrane deformation and DNA damage [180,181]. Vietri and co-workers suggest that the ESCRT III machinery is a “double-edged sword”, driving repair and compartmentalization in wildtype conditions but performing as a damaging agent in dysfunctional conditions [179]. ESCRT III subunits have been also implicated in the regulation of nuclear envelope channels, which contribute to the reintegration of chromosome fragments into the nuclei, impacting genome integrity [182,183]. Another aspect of the role of the ESCRT machinery in nuclear envelope dynamics is also suggested by a study focusing on nuclear invaginations. Here, using *C. elegans* as a model system, the authors demonstrate how, in the early phase of organismal development, the ESCRT machinery contributes to nuclear membrane remodeling and to the preservation of genome integrity [184].

Two seminal papers have described the role of the ESCRT machinery in preserving the intertwined integrity of the nuclear rim in the interphase and that of the genome. Denais et al. and Raab et al. showed that mechanically stressed nuclei lose their circularity and display nuclear blebs, where the ESCRT III subunits accumulate [7,8]. These studies showed that ESCRT III-mediated repair is needed for preserving the genome from DNA damage and opened the route to an area of research focusing on the direct mechanistic relationship between the ESCRT machinery and genome fragility in a clinical perspective as well.

#### 2.4. Nuclear ESCRTs and Disease

The role of ESCRT subunits as guardians of nuclear envelope integrity inevitably ties their dysfunction to pathological situations affecting the nucleus and its genomic content. Failed nuclear envelope repair in the interphase after rupture or in the terminal phase of mitosis leads, as described, to altered genome organization, DNA migration out of the nucleus, and DNA exposure to enzymes that alter if not prevent its function, which induces the pathological state of the cell and of the organism.

From a mechanical perspective, the fragility of the nuclear membrane and/or the disorganization of chromatin decrease the nuclear and cellular resilience to stress [185,186]. This latter aspect becomes particularly relevant in the context of pathologies characterized by fragile nuclei. An example is Hutchinson Gilford Progeria Syndrome, which is linked to a mutation in the LMNA gene, which leads to the production of a truncated, aberrant, and not properly matured form of lamin A that phenotypically generates deformed nuclei displaying surface blebs, a disorganized genome, and an altered distribution of nuclear proteins dependent on the lamin meshwork. It is not surprising that, in this context, the modulation of ESCRT subunits impact the phenotype [187].

Moreover, the role exerted by the ESCRT machinery at the nuclear envelope impacts tumor aggressiveness in the metastasis process (reviewed in [188,189]). In fact, when tumor cells undergo migration through tight interstitial spaces within tissues, they necessitate the significant deformation of both the cell and its nucleus as also shown by Denais et al. in studies investigating mammalian tumor cell migration within confined microenvironments [8].

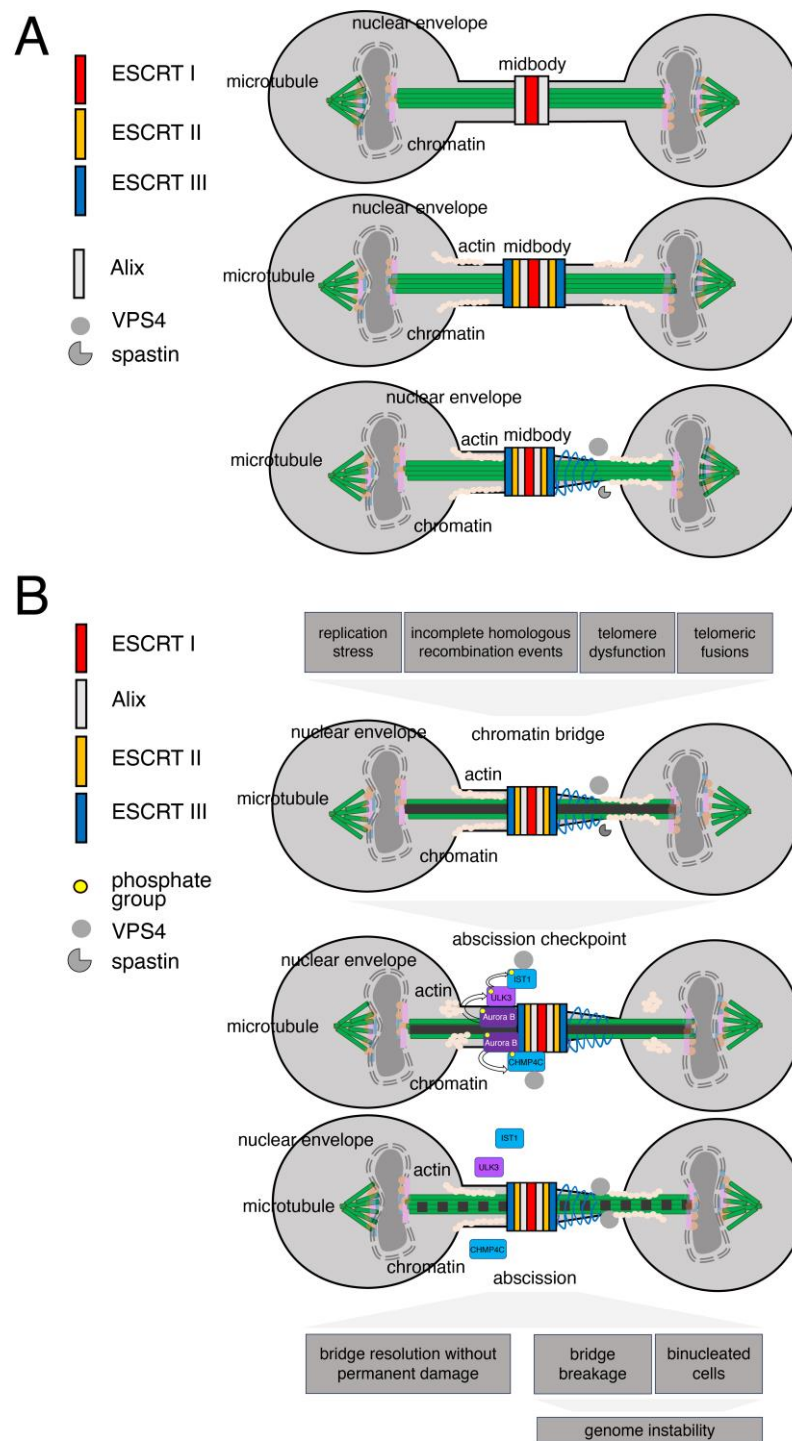
### 3. The ESCRT Machinery and Genome Integrity at the Midbody

#### 3.1. Cell Abscission and ESCRT Complexes

Cytokinesis is a multistep process that permits the correct physical separation of daughter cells following nuclear division. It includes the assembly of the actomyosin contractile actin ring to achieve a primary constriction leading to the formation of the intercellular bridge between the two daughter cells, the physical reorganization of microtubules during bridge formation, and the secondary constriction of the intercellular bridge, ending with the final abscission step [190] (Figure 4A). The ESCRT machinery functions at the heart of cell abscission and orchestrates membrane fission events. It operates in abscission via the sequential assembly of ESCRT I, II, and III subunits at the midbody, the central region of the intercellular bridge that links the daughter cells prior to their separation. The process of ESCRT assembly at this site is initiated by the central spindlin subunit MKLP1 and by CEP55 [191,192]. CEP55 is responsible for the recruitment of the ESCRT I component TSG101 and of the accessory ESCRT ALIX [1,10,193]. The ESCRT I component TSG101 is found at the midbody in association with septins and with AKTIP [71,194]. Recent studies in CEP55-knockout mice have shown that ESCRT recruitment at the midbody can occur also via CEP55-independent mechanisms [195]. Along the same line, *Drosophila* has no CEP55, and ESCRT recruitment to the midbody is mediated by the human MKLP1 orthologue [70].

The microscopical analysis at a 100 to 200 nanometer resolution scale has permitted the visualization of the ESCRT super-structures, which form at the midbody and evolve through the different phases of abscission [196–198]. In the early phase, the ESCRT I and II subunits form packed circular structures at the center of the midbody [194]. ALIX and ESCRT II subunits form double rings next to the central midbody [199]. ESCRT III subunits, including CHMP2A, CHMP4B, and IST1, form double rings at the two sides of the ESCRT I/II structures [200,201]. The TSG101 homologue AKTIP locates at the midbody, forming a ring in the central zone of the bridge, in close association with TSG101 and in proximity to ESCRT III subunits [71]. In the late phase of abscission, the ESCRT III rings are transformed into spirals leading to the completeness of cell division [196,200,202]. This latter process depends on the ATPase VPS4 [39,203]. In this final phase, CHMP1B-dependent recruitment of the ATPase spastin occurs to finalize the intercellular bridge microtubule severing [62–204].





**Figure 4.** ESCRT recruitment and function in abscission. **(A)** Schematic of the midbody during abscission in which ESCRT I (red) and ALIX (light grey) are recruited at the middle of the tubulin (green) bridge by central spindlin and CEP55. ESCRT I and ALIX recruit ESCRT III subunits (blue). In the final stage of abscission, the ESCRT III subunits form spirals (blue spirals) and recruit spastin, which trims the microtubules, and VPS24. **(B)** Schematic representation of the abscission checkpoint activation triggered by the presence of a chromatin bridge (dark grey line). Phosphorylation (curved arrow); proteins recruited at core region of chromatin (light pink rectangle, light orange circle, light blue rectangle); actin (white circles in line and organized in patches).

### 3.2. Abscission Check Point and Chromosome Integrity

The completion of abscission must be intimately coordinated with the correct chromosome distribution into the daughter cells, which preestablishes an interlink between chromosome and genome integrity on one side and the activity of the ESCRT machinery at the intercellular bridge on the other. Actually, chromosome segregation and ESCRT activity during abscission are commonly controlled by a checkpoint [205,206]. This abscission checkpoint is present in budding yeast (NoCut) and involves the kinase IPL1/Aurora [207,208]. In human cells, the kinase Aurora B controls the checkpoint guiding the localization and function of ATPases at the midbody [209]. Aurora B localizes to the midbody in the telophase inside the central region (or Flemming body) [209,210], where it targets CHMP4C and VPS4 [211–213]. Consistently, when the expression of Aurora B is reduced, the localization of the ESCRT III CHMP4C is altered [214].

The abscission checkpoint is driven by stresses, among which the most studied is the presence of anaphase chromatin bridges in association with chromosome integrity [215]. Stretches of DNA linking the two daughter cell genomes can be driven by replication defects, by incomplete homologous recombination events, or by telomere dysfunction and telomeric fusions [216–220]. DNA bridges are divided into ordinary and ultrafine. The latter are detected exclusively by staining the associated proteins, while ordinary DNA bridges are visible with conventional DNA staining methods [221,222]. Aurora B localizes at the midbody in response to the presence of these chromatin bridges (Figure 4B). Its recruitment is controlled by the Mre11-Rad50-Nbs1 (MRN) complex, the DNA double-strand break signaling kinase ATM, and its target CHK2 [223]. To revert Aurora B activity and overcome the abscission checkpoint, specialized factors localize at the midbody as RIF1 and PP1 $\gamma$  and PKC $\epsilon$  [214,224,225]. The data suggest that RIF1 and PP1 $\gamma$  counteract Aurora B dependent phosphorylation of the ESCRT subunit CHMP4C [224]. The kinase ULK3, whose ESCRT target is IST1, also localizes at the midbody and controls abscission [226].

In parallel, to protect and stabilize chromosome bridges, cells reduce the depolymerization of actin filaments at the bridge and produce actin patches at either side of the bridge [227]. These latter structures could contribute to reducing the tension at the bridges by counteracting the velocity by which the daughter cells move when separating from each other [228]. Importantly, actin delays recruitment of ESCRT III proteins at the abscission site [229].

The abscission checkpoint bodies, consisting of cytoplasmic elements containing phosphorylated Aurora B, CHMP4C, CHMP4B, and ALIX, are a further element in the abscission picture, whose mechanistic role is yet to be fully unraveled [230].

Notwithstanding the abundant control of the abscission timing and the protection of chromatin bridges, the outcome of cytokinesis in the presence of these structures can be detrimental for genome integrity (Figure 4B). While in the best-case scenario stable chromatin bridges can be resolved without permanent DNA damage, unstable bridges and abscission control defects can lead to chromatin breakage, DNA damage, breakage–fusion–bridge cycles, and kataegis and chromothripsis [219,231,232]. In this latter process, clusters of localized rearrangements are randomly reassembled by DNA repair or aberrant DNA replication generating profound genome alterations [233]. Chromatin bridges can also lead to cleavage furrow regression, tetraploid cells, and chromosomal instability [234,235]. The cytoplasmic exonuclease TREX1 has also been implicated in cleaving chromosome bridges [219,236]. Finally, the presence of chromatin bridges also drives the production of micronuclei containing bridge DNA [237–239].

### 3.3. Abscission Defects and Cancer

The precise determinants of the destiny of chromosomal bridges are yet to be unraveled. It is not yet fully understood what drives chromatin bridge breakage or furrow regression. In either case, the presence of chromatin bridges and abscission checkpoint defects are drivers of genomic alterations and chromosome instability and are associated with cancer development and/or aggressiveness [240–242]. This highlights the importance of ex-

ploring the properties of ESCRT subunits for the understanding of new molecular cascades driving cancer and to identify new therapeutic targets. Several studies have already given insights into this perspective. The increase in Aurora B expression, for example, has been described in several tumor types and is associated with unfavorable prognosis [243–245]. Moreover, a CHMP4C polymorphism impairing ALIX-binding activity, has been associated with ovarian cancer [246,247].

#### 4. Conclusions

Both for its role in the abscission process and in safeguarding the integrity of the nuclear membrane of mitotic and interphase cells, the ESCRT machinery profoundly impacts the correct organization of the genome and the dysfunction that ensues. By directly repairing breaches in the nuclear membrane, by controlling the abscission process, and, indirectly, by influencing genome organization, the machinery has a strong impact on cellular resilience and organismal pathologies. For future studies in the field, it will be interesting to reflect on the continuum of events linking the final stages of nuclear membrane organization and the cleavage of the bridge linking nuclei exiting division. It is possible that with a dynamic analysis of these events, enabled by modern cytological analysis tools, new interpretations can be offered.

Finally, an aspect deserving further study is the potential identification of individual ESCRT components as therapeutic targets or tools. This can be achieved either by targeting synthetic lethal dependencies, as already demonstrated for VPS4, or by correcting expression defects [248,249]. In either case, the genes themselves or molecules that control/mimic their expression can provide new therapeutic avenues to explore in various pathological contexts.

**Author Contributions:** I.S., conceptualization and writing; M.L.T. and R.B., writing and editing; I.S., funding acquisition. All authors have read and agreed to the published version of the manuscript.

**Funding:** The authors acknowledge the support of NBFC to I.S., funded by the National Recovery and Resilience Plan (NRRP), Mission 4 Component 2 Investment 1.4—Call for tender No. 3138 of 16 December 2021, rectified by Decree n. 3175 of 18 December 2021 of the Italian Ministry of University and Research funded by the European Union—NextGenerationEU; Award Number: Pro, Project code CN\_00000033, Concession Decree No. 1034 of 17 June 2022, adopted by the Italian Ministry of University and Research, Project title “National Biodiversity Future Center—NBFC” Sapienza CN5-Spoke 7. AIRC IG-24614 to I.S. Istituto Pasteur Fondazione Cenci Bolognetti Anna Tramontano call 2020 to I.S. MUR-Sapienza, (RP12218167BDB0A9, RP123188DE994577) to I.S. MUR-Sapienza RM12117A5D970AB9 and GA122181AFEB4283 to I.S. as co-PI. Italian ministry of health 2022 Programma di ricerca e formazione to IS. Singapore ministry of health HLCA22Feb-0029 to I.S. as co-PI. I.S. is affiliated with the following institutions: School of Biological Sciences, Nanyang Technological University, Singapore; NISB Institute of Structural Biology, Nanyang Technological University, Singapore; CNR Institute of Molecular Biology and Pathology, Rome, Italy; Istituto Pasteur Fondazione Cenci Bolognetti, Rome, Italy.

**Conflicts of Interest:** The authors declare no conflicts of interest. The funders had no role in the writing of the manuscript.

#### References

1. Morita, E.; Sandrin, V.; Chung, H.Y.; Morham, S.G.; Gygi, S.P.; Rodesch, C.K.; Sundquist, W.I. Human ESCRT and ALIX proteins interact with proteins of the midbody and function in cytokinesis. *EMBO J.* **2007**, *26*, 4215–4227. [[CrossRef](#)] [[PubMed](#)]
2. Katzmann, D.J.; Babst, M.; Emr, S.D. Ubiquitin-dependent sorting into the multivesicular body pathway requires the function of a conserved endosomal protein sorting complex, ESCRT-I. *Cell* **2001**, *106*, 145–155. [[CrossRef](#)] [[PubMed](#)]
3. Loncle, N.; Agromayor, M.; Martin-Serrano, J.; Williams, D.W. An ESCRT module is required for neuron pruning. *Sci. Rep.* **2015**, *5*, 8461. [[CrossRef](#)]
4. Zhang, H.; Wang, Y.; Wong, J.J.; Lim, K.L.; Liou, Y.C.; Wang, H.; Yu, F. Endocytic pathways downregulate the L1-type cell adhesion molecule neuroglian to promote dendrite pruning in *Drosophila*. *Dev. Cell* **2014**, *30*, 463–478. [[CrossRef](#)] [[PubMed](#)]
5. Vietri, M.; Schink, K.O.; Campsteijn, C.; Wegner, C.S.; Schultz, S.W.; Christ, L.; Thoresen, S.B.; Brech, A.; Raiborg, C.; Stenmark, H. Spastin and ESCRT-III coordinate mitotic spindle disassembly and nuclear envelope sealing. *Nature* **2015**, *522*, 231–235. [[CrossRef](#)] [[PubMed](#)]

6. Olmos, Y.; Hodgson, L.; Mantell, J.; Verkade, P.; Carlton, J.G. ESCRT-III controls nuclear envelope reformation. *Nature* **2015**, *522*, 236–239. [[CrossRef](#)] [[PubMed](#)]
7. Raab, M.; Gentili, M.; de Belly, H.; Thiam, H.R.; Vargas, P.; Jimenez, A.J.; Lautenschlaeger, F.; Voituriez, R.; Lennon-Dumenil, A.M.; Manel, N.; et al. ESCRT III repairs nuclear envelope ruptures during cell migration to limit DNA damage and cell death. *Science* **2016**, *352*, 359–362. [[CrossRef](#)] [[PubMed](#)]
8. Denais, C.M.; Gilbert, R.M.; Isermann, P.; McGregor, A.L.; te Lindert, M.; Weigelin, B.; Davidson, P.M.; Friedl, P.; Wolf, K.; Lammerding, J. Nuclear envelope rupture and repair during cancer cell migration. *Science* **2016**, *352*, 353–358. [[CrossRef](#)] [[PubMed](#)]
9. Jimenez, A.J.; Maiuri, P.; Lafaurie-Janvore, J.; Divoux, S.; Piel, M.; Perez, F. ESCRT machinery is required for plasma membrane repair. *Science* **2014**, *343*, 1247136. [[CrossRef](#)]
10. Carlton, J.G.; Martin-Serrano, J. Parallels between cytokinesis and retroviral budding: A role for the ESCRT machinery. *Science* **2007**, *316*, 1908–1912. [[CrossRef](#)]
11. Votteler, J.; Sundquist, W.I. Virus budding and the ESCRT pathway. *Cell Host Microbe* **2013**, *14*, 232–241. [[CrossRef](#)] [[PubMed](#)]
12. Martin-Serrano, J.; Eastman, S.W.; Chung, W.; Bieniasz, P.D. HECT ubiquitin ligases link viral and cellular PPXY motifs to the vacuolar protein-sorting pathway. *J. Cell Biol.* **2005**, *168*, 89–101. [[CrossRef](#)] [[PubMed](#)]
13. Garrus, J.E.; von Schwedler, U.K.; Pornillos, O.W.; Morham, S.G.; Zavitz, K.H.; Wang, H.E.; Wettstein, D.A.; Stray, K.M.; Cote, M.; Rich, R.L.; et al. Tsg101 and the vacuolar protein sorting pathway are essential for HIV-1 budding. *Cell* **2001**, *107*, 55–65. [[CrossRef](#)] [[PubMed](#)]
14. Vietri, M.; Radulovic, M.; Stenmark, H. The many functions of ESCRTs. *Nat. Rev. Mol. Cell Biol.* **2020**, *21*, 25–42. [[CrossRef](#)] [[PubMed](#)]
15. Morita, E.; Sandrin, V.; Alam, S.L.; Eckert, D.M.; Gygi, S.P.; Sundquist, W.I. Identification of human MVB12 proteins as ESCRT-I subunits that function in HIV budding. *Cell Host Microbe* **2007**, *2*, 41–53. [[CrossRef](#)] [[PubMed](#)]
16. Kostelansky, M.S.; Sun, J.; Lee, S.; Kim, J.; Ghirlando, R.; Hierro, A.; Emr, S.D.; Hurley, J.H. Structural and functional organization of the ESCRT-I trafficking complex. *Cell* **2006**, *125*, 113–126. [[CrossRef](#)] [[PubMed](#)]
17. Hierro, A.; Sun, J.; Rusnak, A.S.; Kim, J.; Prag, G.; Emr, S.D.; Hurley, J.H. Structure of the ESCRT-II endosomal trafficking complex. *Nature* **2004**, *431*, 221–225. [[CrossRef](#)] [[PubMed](#)]
18. Saksena, S.; Wahlman, J.; Teis, D.; Johnson, A.E.; Emr, S.D. Functional reconstitution of ESCRT-III assembly and disassembly. *Cell* **2009**, *136*, 97–109. [[CrossRef](#)] [[PubMed](#)]
19. Williams, R.L.; Urbe, S. The emerging shape of the ESCRT machinery. *Nat. Rev. Mol. Cell Biol.* **2007**, *8*, 355–368. [[CrossRef](#)]
20. Raiborg, C.; Bache, K.G.; Gilooley, D.J.; Madshus, I.H.; Stang, E.; Stenmark, H. Hrs sorts ubiquitinated proteins into clathrin-coated microdomains of early endosomes. *Nat. Cell Biol.* **2002**, *4*, 394–398. [[CrossRef](#)]
21. Bishop, N.; Woodman, P. TSG101/mammalian VPS23 and mammalian VPS28 interact directly and are recruited to VPS4-induced endosomes. *J. Biol. Chem.* **2001**, *276*, 11735–11742. [[CrossRef](#)] [[PubMed](#)]
22. Stuchell, M.D.; Garrus, J.E.; Muller, B.; Stray, K.M.; Ghaffarian, S.; McKinnon, R.; Krausslich, H.G.; Morham, S.G.; Sundquist, W.I. The human endosomal sorting complex required for transport (ESCRT-I) and its role in HIV-1 budding. *J. Biol. Chem.* **2004**, *279*, 36059–36071. [[CrossRef](#)] [[PubMed](#)]
23. Bache, K.G.; Slagsvold, T.; Cabezas, A.; Rosendal, K.R.; Raiborg, C.; Stenmark, H. The growth-regulatory protein HCRP1/hVps37A is a subunit of mammalian ESCRT-I and mediates receptor down-regulation. *Mol. Biol. Cell* **2004**, *15*, 4337–4346. [[CrossRef](#)] [[PubMed](#)]
24. Eastman, S.W.; Martin-Serrano, J.; Chung, W.; Zang, T.; Bieniasz, P.D. Identification of human VPS37C, a component of endosomal sorting complex required for transport-I important for viral budding. *J. Biol. Chem.* **2005**, *280*, 628–636. [[CrossRef](#)] [[PubMed](#)]
25. Oestreich, A.J.; Davies, B.A.; Payne, J.A.; Katzmann, D.J. Mvb12 is a novel member of ESCRT-I involved in cargo selection by the multivesicular body pathway. *Mol. Biol. Cell* **2007**, *18*, 646–657. [[CrossRef](#)] [[PubMed](#)]
26. Babst, M.; Katzmann, D.J.; Snyder, W.B.; Wendland, B.; Emr, S.D. Endosome-associated complex, ESCRT-II, recruits transport machinery for protein sorting at the multivesicular body. *Dev. Cell* **2002**, *3*, 283–289. [[CrossRef](#)] [[PubMed](#)]
27. Teo, H.; Gill, D.J.; Sun, J.; Perisic, O.; Veprintsev, D.B.; Vallis, Y.; Emr, S.D.; Williams, R.L. ESCRT-I core and ESCRT-II GLUE domain structures reveal role for GLUE in linking to ESCRT-I and membranes. *Cell* **2006**, *125*, 99–111. [[CrossRef](#)] [[PubMed](#)]
28. Slagsvold, T.; Aasland, R.; Hirano, S.; Bache, K.G.; Raiborg, C.; Trambaiolo, D.; Wakatsuki, S.; Stenmark, H. Eap45 in mammalian ESCRT-II binds ubiquitin via a phosphoinositide-interacting GLUE domain. *J. Biol. Chem.* **2005**, *280*, 19600–19606. [[CrossRef](#)]
29. Babst, M.; Katzmann, D.J.; Estepa-Sabal, E.J.; Meerloo, T.; Emr, S.D. Escrt-III: An endosome-associated heterooligomeric protein complex required for mvb sorting. *Dev. Cell* **2002**, *3*, 271–282. [[CrossRef](#)]
30. Peck, J.W.; Bowden, E.T.; Burbelo, P.D. Structure and function of human Vps20 and Snf7 proteins. *Biochem. J.* **2004**, *377*, 693–700. [[CrossRef](#)]
31. Yorikawa, C.; Shibata, H.; Waguri, S.; Hatta, K.; Horii, M.; Katoh, K.; Kobayashi, T.; Uchiyama, Y.; Maki, M. Human CHMP6, a myristoylated ESCRT-III protein, interacts directly with an ESCRT-II component EAP20 and regulates endosomal cargo sorting. *Biochem. J.* **2005**, *387 Pt 1*, 17–26. [[CrossRef](#)] [[PubMed](#)]
32. Morita, E.; Colf, L.A.; Karren, M.A.; Sandrin, V.; Rodesch, C.K.; Sundquist, W.I. Human ESCRT-III and VPS4 proteins are required for centrosome and spindle maintenance. *Proc. Natl. Acad. Sci. USA* **2010**, *107*, 12889–12894. [[CrossRef](#)]



33. Adell, M.A.; Vogel, G.F.; Pakdel, M.; Muller, M.; Lindner, H.; Hess, M.W.; Teis, D. Coordinated binding of Vps4 to ESCRT-III drives membrane neck constriction during MVB vesicle formation. *J. Cell Biol.* **2014**, *205*, 33–49. [[CrossRef](#)]
34. Horii, M.; Shibata, H.; Kobayashi, R.; Katoh, K.; Yorikawa, C.; Yasuda, J.; Maki, M. CHMP7, a novel ESCRT-III-related protein, associates with CHMP4b and functions in the endosomal sorting pathway. *Biochem. J.* **2006**, *400*, 23–32. [[CrossRef](#)]
35. Gu, M.; LaJoie, D.; Chen, O.S.; von Appen, A.; Ladinsky, M.S.; Redd, M.J.; Nikolova, L.; Bjorkman, P.J.; Sundquist, W.I.; Ullman, K.S.; et al. LEM2 recruits CHMP7 for ESCRT-mediated nuclear envelope closure in fission yeast and human cells. *Proc. Natl. Acad. Sci. USA* **2017**, *114*, E2166–E2175. [[CrossRef](#)]
36. Olmos, Y.; Perdrix-Rosell, A.; Carlton, J.G. Membrane Binding by CHMP7 Coordinates ESCRT-III-Dependent Nuclear Envelope Reformation. *Curr. Biol.* **2016**, *26*, 2635–2641. [[CrossRef](#)] [[PubMed](#)]
37. Odorizzi, G. The multiple personalities of Alix. *J. Cell Sci.* **2006**, *119 Pt 15*, 3025–3032. [[CrossRef](#)]
38. Bajorek, M.; Morita, E.; Skalicky, J.J.; Morham, S.G.; Babst, M.; Sundquist, W.I. Biochemical analyses of human IST1 and its function in cytokinesis. *Mol. Biol. Cell* **2009**, *20*, 1360–1373. [[CrossRef](#)] [[PubMed](#)]
39. Mierzwa, B.E.; Chiaruttini, N.; Redondo-Morata, L.; von Filseck, J.M.; Konig, J.; Larios, J.; Poser, I.; Muller-Reichert, T.; Scheuring, S.; Roux, A.; et al. Dynamic subunit turnover in ESCRT-III assemblies is regulated by Vps4 to mediate membrane remodelling during cytokinesis. *Nat. Cell Biol.* **2017**, *19*, 787–798. [[CrossRef](#)]
40. Bilodeau, P.S.; Winistorfer, S.C.; Kearney, W.R.; Robertson, A.D.; Piper, R.C. Vps27-Hse1 and ESCRT-I complexes cooperate to increase efficiency of sorting ubiquitinated proteins at the endosome. *J. Cell Biol.* **2003**, *163*, 237–243. [[CrossRef](#)]
41. Huang, H.-R.; Chen, Z.J.; Kunes, S.; Chang, G.-D.; Maniatis, T. Endocytic pathway is required for *Drosophila* Toll innate immune signaling. *Proc. Natl. Acad. Sci. USA* **2010**, *107*, 8322–8327. [[CrossRef](#)] [[PubMed](#)]
42. Chanut-Delalande, H.; Jung, A.C.; Baer, M.M.; Lin, L.; Payre, F.; Affolter, M. The Hrs/Stam complex acts as a positive and negative regulator of RTK signaling during *Drosophila* development. *PLoS ONE* **2010**, *5*, e10245. [[CrossRef](#)] [[PubMed](#)]
43. Kojima, K.; Amano, Y.; Yoshino, K.; Tanaka, N.; Sugamura, K.; Takeshita, T. ESCRT-0 protein hepatocyte growth factor-regulated tyrosine kinase substrate (Hrs) is targeted to endosomes independently of signal-transducing adaptor molecule (STAM) and the complex formation with STAM promotes its endosomal dissociation. *J. Biol. Chem.* **2014**, *289*, 33296–33310. [[CrossRef](#)] [[PubMed](#)]
44. Kostelansky, M.S.; Schluter, C.; Tam, Y.Y.; Lee, S.; Ghirlando, R.; Beach, B.; Conibear, E.; Hurley, J.H. Molecular architecture and functional model of the complete yeast ESCRT-I heterotetramer. *Cell* **2007**, *129*, 485–498. [[CrossRef](#)] [[PubMed](#)]
45. Moberg, K.H.; Schelble, S.; Burdick, S.K.; Hariharan, I.K. Mutations in erupted, the *Drosophila* ortholog of mammalian tumor susceptibility Gene 101, elicit non-cell-autonomous overgrowth. *Dev. Cell* **2005**, *9*, 699–710. [[CrossRef](#)] [[PubMed](#)]
46. Sevrioukov, E.A.; Moghrabi, N.; Kuhn, M.; Kramer, H. A mutation in dVps28 reveals a link between a subunit of the endosomal sorting complex required for transport-I complex and the actin cytoskeleton in *Drosophila*. *Mol. Biol. Cell* **2005**, *16*, 2301–2312. [[CrossRef](#)] [[PubMed](#)]
47. Vaccari, T.; Rusten, T.E.; Menut, L.; Nezis, I.P.; Brech, A.; Stenmark, H.; Bilder, D. Comparative analysis of ESCRT-I, ESCRT-II and ESCRT-III function in *Drosophila* by efficient isolation of ESCRT mutants. *J. Cell Sci.* **2009**, 2413–2423. [[CrossRef](#)] [[PubMed](#)]
48. Hodgson, J.J.; Buchon, N.; Blissard, G.W. Identification of Cellular Genes Involved in Baculovirus GP64 Trafficking to the Plasma Membrane. *J. Virol.* **2022**, *96*, e0021522. [[CrossRef](#)] [[PubMed](#)]
49. Li, Z.; Blissard, G. The vacuolar protein sorting genes in insects: A comparative genome view. *Insect Biochem. Mol. Biol.* **2015**, *62*, 211–225. [[CrossRef](#)]
50. Yang, X.; Mao, F.; Lv, X.; Zhang, Z.; Fu, L.; Lu, Y.; Wu, W.; Zhou, Z.; Zhang, L.; Zhao, Y. *Drosophila* Vps36 regulates Smo trafficking in Hedgehog signaling. *Development* **2013**, *126*, e2008. [[CrossRef](#)]
51. Herz, H.-M.; Woodfield, S.E.; Chen, Z.; Bolduc, C.; Bergmann, A. Common and distinct genetic properties of ESCRT-II components in *Drosophila*. *PLoS ONE* **2009**, *4*, e4165. [[CrossRef](#)]
52. Thompson, B.J.; Mathieu, J.; Sung, H.-H.; Loeser, E.; Rørth, P.; Cohen, S.M. Tumor suppressor properties of the ESCRT-II complex component Vps25 in *Drosophila*. *Dev. Cell* **2005**, *9*, 711–720. [[CrossRef](#)] [[PubMed](#)]
53. Irion, U.; St Johnston, D. *bicoid* RNA localization requires specific binding of an endosomal sorting complex. *Nature* **2007**, *445*, 554–558. [[CrossRef](#)]
54. Bauer, I.; Brune, T.; Preiss, R.; Kölling, R. Evidence for a Nonendosomal Function of the *Saccharomyces cerevisiae* ESCRT-III-Like Protein Chm7. *Genetics* **2015**, *201*, 1439–1452. [[CrossRef](#)]
55. Webster, B.M.; Thaller, D.J.; Jäger, J.; Ochmann, S.E.; Borah, S.; Lusk, C.P. Chm7 and Heh1 collaborate to link nuclear pore complex quality control with nuclear envelope sealing. *EMBO J.* **2016**, *35*, 2447–2467. [[CrossRef](#)]
56. Aoyama, N.; Yamakawa, T.; Sasamura, T.; Yoshida, Y.; Ohori, M.; Okubo, H.; Iida, E.; Sasaki, N.; Ueda, R.; Matsuno, K. Loss- and gain-of-function analyses of vacuolar protein sorting 2 in Notch signaling of *Drosophila melanogaster*. *Gen. Genet. Syst.* **2013**, *88*, 45–57. [[CrossRef](#)] [[PubMed](#)]
57. Jan, Y.N.; Sweeney, N.; Brenman, J.; Gao, F.-B. The coiled-coil protein shrub controls neuronal morphogenesis in *Drosophila*. *Curr. Biol.* **2006**, *16*, 1006–1011.
58. Troost, T.; Jaekel, S.; Ohlenhard, N.; Klein, T. The tumour suppressor Lethal (2) giant discs is required for the function of the ESCRT-III component Shrub/CHMP4. *J. Cell Sci.* **2012**, *125*, 763–776. [[CrossRef](#)]
59. Dimaano, C.; Jones, C.B.; Hanono, A.; Curtiss, M.; Babst, M. Ist1 regulates Vps4 localization and assembly. *Mol. Biol. Cell* **2008**, *19*, 465–474. [[CrossRef](#)]



60. Bäumers, M.; Klose, S.; Brüser, C.; Haag, C.; Hänsch, S.; Pannen, H.; Weidtkamp-Peters, S.; Feldbrügge, M.; Klein, T. The auxiliary ESCRT complexes provide robustness to cold in poikilothermic organisms. *Biol. Open* **2019**, *8*. [[CrossRef](#)]
61. Marie, P.P.; Fan, S.; Mason, J.; Wells, A.; Mendes, C.C.; Wainwright, S.M.; Scott, S.; Fischer, R.; Harris, A.L.; Wilson, C.; et al. Accessory ESCRT-III proteins are conserved and selective regulators of Rab11a-exosome formation. *J. Extracell. Vesicles* **2023**, *12*, e12311. [[CrossRef](#)] [[PubMed](#)]
62. Reid, E.; Connell, J.; Edwards, T.L.; Duley, S.; Brown, S.E.; Sanderson, C.M. The hereditary spastic paraplegia protein spastin interacts with the ESCRT-III complex-associated endosomal protein CHMP1B. *Hum. Mol. Genet.* **2005**, *14*, 19–38. [[CrossRef](#)] [[PubMed](#)]
63. Yang, D.; Rismanchi, N.; Renvoise, B.; Lippincott-Schwartz, J.; Blackstone, C.; Hurley, J.H. Structural basis for midbody targeting of spastin by the ESCRT-III protein CHMP1B. *Nat. Struct. Mol. Biol.* **2008**, *15*, 1278–1286. [[CrossRef](#)] [[PubMed](#)]
64. Babst, M.; Wendland, B.; Estepa, E.J.; Emr, S.D. The Vps4p AAA ATPase regulates membrane association of a Vps protein complex required for normal endosome function. *EMBO J.* **1998**, *17*, 2982–2993. [[CrossRef](#)] [[PubMed](#)]
65. Rusten, T.E.; Vaccari, T.; Lindmo, K.; Rodahl, L.M.; Nezis, I.P.; Sem-Jacobsen, C.; Wendler, F.; Vincent, J.-P.; Brech, A.; Bilder, D.; et al. ESCRTs and Fab1 regulate distinct steps of autophagy. *Curr. Biol.* **2007**, *17*, 1817–1825. [[CrossRef](#)] [[PubMed](#)]
66. Shen, J.; Yang, Z.; Wang, J.; Zhao, B.; Lan, W.; Wang, C.; Zhang, X.; Wild, C.J.; Liu, M.; Xu, Z.; et al. NMR studies on the interactions between yeast Vta1 and Did2 during the multivesicular bodies sorting pathway. *Sci. Rep.* **2016**, *6*, 38710. [[CrossRef](#)]
67. Eikenes, Å.H.; Malerød, L.; Christensen, A.L.; Steen, C.B.; Mathieu, J.; Nezis, I.P.; Liestøl, K.; Huynh, J.-R.; Stenmark, H.; Haglund, K. ALIX and ESCRT-III coordinately control cytokinetic abscission during germline stem cell division in vivo. *PLoS Genet.* **2015**, *11*, e1004904. [[CrossRef](#)] [[PubMed](#)]
68. Skalicky, J.J.; Arii, J.; Wenzel, D.M.; Stubblefield, W.-M.B.; Katsuyama, A.; Uter, N.T.; Bajorek, M.; Myszka, D.G.; Sundquist, W.I. Interactions of the human LIP5 regulatory protein with endosomal sorting complexes required for transport. *J. Biol. Chem.* **2012**, *287*, 43910–43926. [[CrossRef](#)]
69. Wemmer, M.; Azmi, I.; West, M.; Davies, B.; Katzmann, D.; Odorizzi, G. Bro1 binding to Snf7 regulates ESCRT-III membrane scission activity in yeast. *J. Cell Biol.* **2011**, *192*, 295–306. [[CrossRef](#)]
70. Lie-Jensen, A.; Ivanauskienė, K.; Malerød, L.; Jain, A.; Tan, K.W.; Laerdahl, J.K.; Liestøl, K.; Stenmark, H.; Haglund, K. Centralspindlin Recruits ALIX to the Midbody during Cytokinetic Abscission in *Drosophila* via a Mechanism Analogous to Virus Budding. *Curr. Biol.* **2019**, *29*, 3538–3548.e7. [[CrossRef](#)]
71. Merigliano, C.; Burla, R.; La Torre, M.; Del Giudice, S.; Teo, H.; Liew, C.W.; Chojnowski, A.; Goh, W.I.; Olmos, Y.; Maccaroni, K.; et al. AKTIP interacts with ESCRT I and is needed for the recruitment of ESCRT III subunits to the midbody. *PLoS Genet.* **2021**, *17*, e1009757. [[CrossRef](#)] [[PubMed](#)]
72. Burla, R.; Carcuro, M.; Raffa, G.D.; Galati, A.; Raimondo, D.; Rizzo, A.; La Torre, M.; Micheli, E.; Ciapponi, L.; Cenci, G.; et al. AKTIP/Ft1, a New Shelterin-Interacting Factor Required for Telomere Maintenance. *PLoS Genet.* **2015**, *11*, e1005167. [[CrossRef](#)] [[PubMed](#)]
73. Burla, R.; Carcuro, M.; Torre, M.L.; Fratini, F.; Crescenzi, M.; D’Apice, M.R.; Spitalieri, P.; Raffa, G.D.; Astrologo, L.; Lattanzi, G.; et al. The telomeric protein AKTIP interacts with A- and B-type lamins and is involved in regulation of cellular senescence. *Open Biol.* **2016**, *6*, 160103. [[CrossRef](#)] [[PubMed](#)]
74. La Torre, M.; Merigliano, C.; Burla, R.; Mottini, C.; Zanetti, G.; Del Giudice, S.; Carcuro, M.; Virdia, I.; Bucciarelli, E.; Manni, I.; et al. Mice with reduced expression of the telomere-associated protein Ft1 develop p53-sensitive progeroid traits. *Aging Cell* **2018**, *17*, e12730. [[CrossRef](#)] [[PubMed](#)]
75. La Torre, M.; Merigliano, C.; Maccaroni, K.; Chojnowski, A.; Goh, W.I.; Giubettini, M.; Verni, F.; Capanni, C.; Rhodes, D.; Wright, G.; et al. Combined alteration of lamin and nuclear morphology influences the localization of the tumor-associated factor AKTIP. *J. Exp. Clin. Cancer Res.* **2022**, *41*, 273. [[CrossRef](#)] [[PubMed](#)]
76. Xu, L.; Sowa, M.E.; Chen, J.; Li, X.; Gygi, S.P.; Harper, J.W. An FTS/Hook/p107(FHIP) complex interacts with and promotes endosomal clustering by the homotypic vacuolar protein sorting complex. *Mol. Biol. Cell* **2008**, *19*, 5059–5071. [[CrossRef](#)]
77. Leung, K.F.; Dacks, J.B.; Field, M.C. Evolution of the multivesicular body ESCRT machinery; retention across the eukaryotic lineage. *Traffic* **2008**, *9*, 1698–1716. [[CrossRef](#)]
78. Hatano, T.; Palani, S.; Papatziadou, D.; Salzer, R.; Souza, D.P.; Tamarit, D.; Makwana, M.; Potter, A.; Haig, A.; Xu, W.; et al. Asgard archaea shed light on the evolutionary origins of the eukaryotic ubiquitin-ESCRT machinery. *Nat. Commun.* **2022**, *13*, 3398. [[CrossRef](#)] [[PubMed](#)]
79. Makarova, K.S.; Tobiasson, V.; Wolf, Y.I.; Lu, Z.; Liu, Y.; Zhang, S.; Krupovic, M.; Li, M.; Koonin, E.V. Diversity, origin, and evolution of the ESCRT systems. *mBio* **2024**, *15*, e0033524. [[CrossRef](#)]
80. Florian, J.R.; DeMatte, S.J.; Sweeder, D.M.; Ordway, R.W.; Kawasaki, F. Genetic analysis of the *Drosophila* ESCRT-III complex protein, VPS24, reveals a novel function in lysosome homeostasis. *PLoS ONE* **2021**, *16*, e0251184. [[CrossRef](#)]
81. Pannen, H.; Rapp, T.; Klein, T. The ESCRT machinery regulates retromer-dependent transcytosis of septate junction components in *Drosophila*. *eLife* **2020**, *9*, e61866. [[CrossRef](#)]
82. Pineda-Molina, E.; Belrhali, H.; Piefer, A.J.; Akula, I.; Bates, P.; Weissenhorn, W. The crystal structure of the C-terminal domain of Vps28 reveals a conserved surface required for Vps20 recruitment. *Traffic* **2006**, *7*, 1007–1016. [[CrossRef](#)]
83. Gill, D.J.; Teo, H.; Sun, J.; Perisic, O.; Veprintsev, D.B.; Emr, S.D.; Williams, R.L. Structural insight into the ESCRT-I/-II link and its role in MVB trafficking. *EMBO J.* **2007**, *26*, 600–612. [[CrossRef](#)] [[PubMed](#)]

84. Muziol, T.; Pineda-Molina, E.; Ravelli, R.B.; Zamborlini, A.; Usami, Y.; Gottlinger, H.; Weissenhorn, W. Structural basis for budding by the ESCRT-III factor CHMP3. *Dev. Cell* **2006**, *10*, 821–830. [[CrossRef](#)] [[PubMed](#)]
85. Aebi, U.; Cohn, J.; Buhle, L.; Gerace, L. The nuclear lamina is a meshwork of intermediate-type filaments. *Nature* **1986**, *323*, 560–564. [[CrossRef](#)] [[PubMed](#)]
86. Shimi, T.; Kittisopikul, M.; Tran, J.; Goldman, A.E.; Adam, S.A.; Zheng, Y.; Jaqaman, K.; Goldman, R.D. Structural organization of nuclear lamins A, C, B1, and B2 revealed by superresolution microscopy. *Mol. Biol. Cell* **2015**, *26*, 4075–4086. [[CrossRef](#)]
87. Ho, C.Y.; Lammerding, J. Lamins at a glance. *J. Cell Sci.* **2012**, *125*, 2087–2093. [[CrossRef](#)] [[PubMed](#)]
88. Dechat, T.; Pflieger, K.; Sengupta, K.; Shimi, T.; Shumaker, D.K.; Solimando, L.; Goldman, R.D. Nuclear lamins: Major factors in the structural organization and function of the nucleus and chromatin. *Gen. Dev.* **2008**, *22*, 832–853. [[CrossRef](#)]
89. Dechat, T.; Gesson, K.; Foisner, R. Lamina-independent lamins in the nuclear interior serve important functions. *Cold Spring Harb. Symp. Quant. Biol.* **2010**, *75*, 533–543. [[CrossRef](#)]
90. Moir, R.D.; Yoon, M.; Khuon, S.; Goldman, R.D. Nuclear lamins A and B1: Different pathways of assembly during nuclear envelope formation in living cells. *J. Cell Biol.* **2000**, *151*, 1155–1168. [[CrossRef](#)]
91. Gesson, K.; Vidak, S.; Foisner, R. Lamina-associated polypeptide (LAP)2 $\alpha$  and nucleoplasmic lamins in adult stem cell regulation and disease. *Semin. Cell Dev. Biol.* **2014**, *29*, 116–124. [[CrossRef](#)] [[PubMed](#)]
92. Beck, M.; Hurt, E. The nuclear pore complex: Understanding its function through structural insight. *Nat. Rev. Mol. Cell Biol.* **2017**, *18*, 73–89. [[CrossRef](#)] [[PubMed](#)]
93. Cronshaw, J.M.; Krutchinsky, A.N.; Zhang, W.; Chait, B.T.; Matunis, M.J. Proteomic analysis of the mammalian nuclear pore complex. *J. Cell Biol.* **2002**, *158*, 915–927. [[CrossRef](#)] [[PubMed](#)]
94. Xie, W.; Chojnowski, A.; Boudier, T.; Lim, J.S.; Ahmed, S.; Ser, Z.; Stewart, C.; Burke, B. A-type Lamins Form Distinct Filamentous Networks with Differential Nuclear Pore Complex Associations. *Curr. Biol.* **2016**, *26*, 2651–2658. [[CrossRef](#)] [[PubMed](#)]
95. Smoyer, C.J.; Katta, S.S.; Gardner, J.M.; Stoltz, L.; McCroskey, S.; Bradford, W.D.; McClain, M.; Smith, S.E.; Slaughter, B.D.; Unruh, J.R.; et al. Analysis of membrane proteins localizing to the inner nuclear envelope in living cells. *J. Cell Biol.* **2016**, *215*, 575–590. [[CrossRef](#)]
96. Konde, E.; Bourgeois, B.; Tellier-Lebegue, C.; Wu, W.; Perez, J.; Caputo, S.; Attanda, W.; Gasparini, S.; Charbonnier, J.B.; Gilquin, B.; et al. Structural analysis of the Smad2-MAN1 interaction that regulates transforming growth factor- $\beta$  signaling at the inner nuclear membrane. *Biochemistry* **2010**, *49*, 8020–8032. [[CrossRef](#)] [[PubMed](#)]
97. Lee, K.K.; Wilson, K.L. All in the family: Evidence for four new LEM-domain proteins Lem2 (NET-25), Lem3, Lem4 and Lem5 in the human genome. *Symp. Soc. Exp. Biol.* **2004**, *56*, 329–339.
98. Cai, M.; Huang, Y.; Ghirlando, R.; Wilson, K.L.; Craigie, R.; Clore, G.M. Solution structure of the constant region of nuclear envelope protein LAP2 reveals two LEM-domain structures: One binds BAF and the other binds DNA. *EMBO J.* **2001**, *20*, 4399–4407. [[CrossRef](#)] [[PubMed](#)]
99. Bione, S.; Maestrini, E.; Rivella, S.; Mancini, M.; Regis, S.; Romeo, G.; Toniolo, D. Identification of a novel X-linked gene responsible for Emery-Dreifuss muscular dystrophy. *Nat. Genet.* **1994**, *8*, 323–327. [[CrossRef](#)]
100. Manilal, S.; Nguyen, T.M.; Sewry, C.A.; Morris, G.E. The Emery-Dreifuss muscular dystrophy protein, emerin, is a nuclear membrane protein. *Hum. Mol. Genet.* **1996**, *5*, 801–808. [[CrossRef](#)]
101. Brachner, A.; Foisner, R. Evolution of LEM proteins as chromatin tethers at the nuclear periphery. *Biochem. Soc. Trans.* **2011**, *39*, 1735–1741. [[CrossRef](#)] [[PubMed](#)]
102. Padmakumar, V.C.; Libotte, T.; Lu, W.; Zaim, H.; Abraham, S.; Noegel, A.A.; Gotzmann, J.; Foisner, R.; Karakesisoglou, I. The inner nuclear membrane protein Sun1 mediates the anchorage of Nesprin-2 to the nuclear envelope. *J. Cell Sci.* **2005**, *118*, 3419–3430. [[CrossRef](#)] [[PubMed](#)]
103. Hodzic, D.M.; Yeater, D.B.; Bengtsson, L.; Otto, H.; Stahl, P.D. Sun2 is a novel mammalian inner nuclear membrane protein. *J. Biol. Chem.* **2004**, *279*, 25805–25812. [[CrossRef](#)]
104. Wilhelmsen, K.; Ketema, M.; Truong, H.; Sonnenberg, A. KASH-domain proteins in nuclear migration, anchorage and other processes. *J. Cell Sci.* **2006**, *119*, 5021–5029. [[CrossRef](#)]
105. Ye, Q.; Worman, H.J. Primary structure analysis and lamin B and DNA binding of human LBR, an integral protein of the nuclear envelope inner membrane. *J. Biol. Chem.* **1994**, *269*, 11306–11311. [[CrossRef](#)]
106. Schuler, E.; Lin, F.; Worman, H.J. Characterization of the human gene encoding LBR, an integral protein of the nuclear envelope inner membrane. *J. Biol. Chem.* **1994**, *269*, 11312–11317. [[CrossRef](#)]
107. Olins, A.L.; Rhodes, G.; Welch, D.B.; Zwerger, M.; Olins, D.E. Lamin B receptor: Multi-tasking at the nuclear envelope. *Nucleus* **2010**, *1*, 53–70. [[CrossRef](#)]
108. Crisp, M.; Liu, Q.; Roux, K.; Rattner, J.B.; Shanahan, C.; Burke, B.; Stahl, P.D.; Hodzic, D. Coupling of the nucleus and cytoplasm: Role of the LINC complex. *J. Cell Biol.* **2006**, *172*, 41–53. [[CrossRef](#)]
109. Wang, N.; Tytell, J.D.; Ingber, D.E. Mechanotransduction at a distance: Mechanically coupling the extracellular matrix with the nucleus. *Nat. Rev. Mol. Cell Biol.* **2009**, *10*, 75–82. [[CrossRef](#)] [[PubMed](#)]
110. Mellad, J.A.; Warren, D.T.; Shanahan, C.M. Nesprins LINC the nucleus and cytoskeleton. *Curr. Opin. Cell Biol.* **2011**, *23*, 47–54. [[CrossRef](#)]

111. Lombardi, M.L.; Jaalouk, D.E.; Shanahan, C.M.; Burke, B.; Roux, K.J.; Lammerding, J. The interaction between nesprins and sun proteins at the nuclear envelope is critical for force transmission between the nucleus and cytoskeleton. *J. Biol. Chem.* **2011**, *286*, 26743–26753. [[CrossRef](#)] [[PubMed](#)]
112. Cremer, T.; Cremer, C.; Schneider, T.; Baumann, H.; Hens, L.; Kirsch-Volders, M. Analysis of chromosome positions in the interphase nucleus of Chinese hamster cells by laser-UV-microirradiation experiments. *Hum. Genet.* **1982**, *62*, 201–209. [[CrossRef](#)] [[PubMed](#)]
113. Cremer, T.; Cremer, C.; Baumann, H.; Luedtke, E.K.; Sperling, K.; Teuber, V.; Zorn, C. Rabl's model of the interphase chromosome arrangement tested in Chinese hamster cells by premature chromosome condensation and laser-UV-microbeam experiments. *Hum. Genet.* **1982**, *60*, 46–56. [[CrossRef](#)] [[PubMed](#)]
114. Lieberman-Aiden, E.; van Berkum, N.L.; Williams, L.; Imakaev, M.; Ragoczy, T.; Telling, A.; Amit, I.; Lajoie, B.R.; Sabo, P.J.; Dorschner, M.O.; et al. Comprehensive mapping of long-range interactions reveals folding principles of the human genome. *Science* **2009**, *326*, 289–293. [[CrossRef](#)] [[PubMed](#)]
115. Sajan, S.A.; Hawkins, R.D. Methods for identifying higher-order chromatin structure. *Annu. Rev. Genom. Hum. Genet.* **2012**, *13*, 59–82. [[CrossRef](#)] [[PubMed](#)]
116. Dixon, J.R.; Selvaraj, S.; Yue, F.; Kim, A.; Li, Y.; Shen, Y.; Hu, M.; Liu, J.S.; Ren, B. Topological domains in mammalian genomes identified by analysis of chromatin interactions. *Nature* **2012**, *485*, 376–380. [[CrossRef](#)] [[PubMed](#)]
117. Pombo, A.; Dillon, N. Three-dimensional genome architecture: Players and mechanisms. *Nat. Rev. Mol. Cell Biol.* **2015**, *16*, 245–257. [[CrossRef](#)]
118. Zuin, J.; Dixon, J.R.; van der Reijden, M.I.; Ye, Z.; Kolovos, P.; Brouwer, R.W.; van de Corput, M.P.; van de Werken, H.J.; Knoch, T.A.; van IJcken, W.F.J.; et al. Cohesin and CTCF differentially affect chromatin architecture and gene expression in human cells. *Proc. Natl. Acad. Sci. USA* **2014**, *111*, 996–1001. [[CrossRef](#)]
119. Guelen, L.; Pagie, L.; Brassat, E.; Meuleman, W.; Faza, M.B.; Talhout, W.; Eussen, B.H.; de Klein, A.; Wessels, L.; de Laat, W.; et al. Domain organization of human chromosomes revealed by mapping of nuclear lamina interactions. *Nature* **2008**, *453*, 948–951. [[CrossRef](#)]
120. Kind, J.; Pagie, L.; Ortabozkoyun, H.; Boyle, S.; de Vries, S.S.; Janssen, H.; Amendola, M.; Nolen, L.D.; Bickmore, W.A.; van Steensel, B. Single-cell dynamics of genome-nuclear lamina interactions. *Cell* **2013**, *153*, 178–192. [[CrossRef](#)]
121. van Steensel, B.; Belmont, A.S. Lamina-Associated Domains: Links with Chromosome Architecture, Heterochromatin, and Gene Repression. *Cell* **2017**, *169*, 780–791. [[CrossRef](#)] [[PubMed](#)]
122. Laguri, C.; Gilquin, B.; Wolff, N.; Romi-Lebrun, R.; Courchay, K.; Callebaut, I.; Worman, H.J.; Zinn-Justin, S. Structural characterization of the LEM motif common to three human inner nuclear membrane proteins. *Structure* **2001**, *9*, 503–511. [[CrossRef](#)] [[PubMed](#)]
123. Martins, S.; Eikvar, S.; Furukawa, K.; Collas, P. HA95 and LAP2 $\beta$  mediate a novel chromatin-nuclear envelope interaction implicated in initiation of DNA replication. *J. Cell Biol.* **2003**, *160*, 177–188. [[CrossRef](#)] [[PubMed](#)]
124. Shimi, T.; Koujin, T.; Segura-Totten, M.; Wilson, K.L.; Haraguchi, T.; Hiraoka, Y. Dynamic interaction between BAF and emerin revealed by FRAP, FLIP, and FRET analyses in living HeLa cells. *J. Struct. Biol.* **2004**, *147*, 31–41. [[CrossRef](#)] [[PubMed](#)]
125. Berk, J.M.; Simon, D.N.; Jenkins-Houk, C.R.; Westerbeck, J.W.; Gronning-Wang, L.M.; Carlson, C.R.; Wilson, K.L. The molecular basis of emerin-emerin and emerin-BAF interactions. *J. Cell Sci.* **2014**, *127*, 3956–3969. [[PubMed](#)]
126. Caputo, S.; Couprie, J.; Duband-Goulet, I.; Konde, E.; Lin, F.; Braud, S.; Gondry, M.; Gilquin, B.; Worman, H.J.; Zinn-Justin, S. The carboxyl-terminal nucleoplasmic region of MAN1 exhibits a DNA binding winged helix domain. *J. Biol. Chem.* **2006**, *281*, 18208–18215. [[CrossRef](#)] [[PubMed](#)]
127. Ye, Q.; Worman, H.J. Interaction between an integral protein of the nuclear envelope inner membrane and human chromodomain proteins homologous to *Drosophila* HP1. *J. Biol. Chem.* **1996**, *271*, 14653–14656. [[CrossRef](#)] [[PubMed](#)]
128. Polioudaki, H.; Kourmouli, N.; Drosou, V.; Bakou, A.; Theodoropoulos, P.A.; Singh, P.B.; Giannakouros, T.; Georgatos, S.D. Histones H3/H4 form a tight complex with the inner nuclear membrane protein LBR and heterochromatin protein 1. *EMBO Rep.* **2001**, *2*, 920–925. [[CrossRef](#)]
129. Makatsori, D.; Kourmouli, N.; Polioudaki, H.; Shultz, L.D.; McLean, K.; Theodoropoulos, P.A.; Singh, P.B.; Georgatos, S.D. The inner nuclear membrane protein lamin B receptor forms distinct microdomains and links epigenetically marked chromatin to the nuclear envelope. *J. Biol. Chem.* **2004**, *279*, 25567–25573. [[CrossRef](#)]
130. Mori, R.; Oliferenko, S. Cell Biology: An Open Solution for Closed Mitosis. *Curr. Biol.* **2020**, *30*, R942–R944. [[CrossRef](#)]
131. Boettcher, B.; Barral, Y. The cell biology of open and closed mitosis. *Nucleus* **2013**, *4*, 160–165. [[CrossRef](#)] [[PubMed](#)]
132. Makarova, M.; Oliferenko, S. Mixing and matching nuclear envelope remodeling and spindle assembly strategies in the evolution of mitosis. *Curr. Opin. Cell Biol.* **2016**, *41*, 43–50. [[CrossRef](#)] [[PubMed](#)]
133. Ungricht, R.; Kutay, U. Mechanisms and functions of nuclear envelope remodelling. *Nat. Rev. Mol. Cell Biol.* **2017**, *18*, 229–245. [[CrossRef](#)] [[PubMed](#)]
134. Borah, S.; Dhanasekaran, K.; Kumar, S. The LEM-ESCRT toolkit: Repair and maintenance of the nucleus. *Front. Cell Dev. Biol.* **2022**, *10*, 989217. [[CrossRef](#)]
135. Guttinger, S.; Laurell, E.; Kutay, U. Orchestrating nuclear envelope disassembly and reassembly during mitosis. *Nat. Rev. Mol. Cell Biol.* **2009**, *10*, 178–191. [[CrossRef](#)] [[PubMed](#)]



136. Linder, M.I.; Kohler, M.; Boersema, P.; Weberruss, M.; Wandke, C.; Marino, J.; Ashiono, C.; Picotti, P.; Antonin, W.; Kutay, U. Mitotic Disassembly of Nuclear Pore Complexes Involves CDK1- and PLK1-Mediated Phosphorylation of Key Interconnecting Nucleoporins. *Dev. Cell* **2017**, *43*, 141–156.e7. [[CrossRef](#)] [[PubMed](#)]
137. Peter, M.; Nakagawa, J.; Doree, M.; Labbe, J.C.; Nigg, E.A. In vitro disassembly of the nuclear lamina and M phase-specific phosphorylation of lamins by cdc2 kinase. *Cell* **1990**, *61*, 591–602. [[CrossRef](#)]
138. Kuga, T.; Nozaki, N.; Matsushita, K.; Nomura, F.; Tomonaga, T. Phosphorylation statuses at different residues of lamin B2, B1, and A/C dynamically and independently change throughout the cell cycle. *Exp. Cell Res.* **2010**, *316*, 2301–2312. [[CrossRef](#)]
139. Georgatos, S.D.; Pyrpasoulou, A.; Theodoropoulos, P.A. Nuclear envelope breakdown in mammalian cells involves stepwise lamina disassembly and microtubule-drive deformation of the nuclear membrane. *J. Cell Sci.* **1997**, *110 Pt 17*, 2129–2140. [[CrossRef](#)]
140. Liu, S.Y.; Ikegami, K. Nuclear lamin phosphorylation: An emerging role in gene regulation and pathogenesis of laminopathies. *Nucleus* **2020**, *11*, 299–314. [[CrossRef](#)]
141. Robinson, J.T.; Wojcik, E.J.; Sanders, M.A.; McGrail, M.; Hays, T.S. Cytoplasmic dynein is required for the nuclear attachment and migration of centrosomes during mitosis in *Drosophila*. *J. Cell Biol.* **1999**, *146*, 597–608. [[CrossRef](#)] [[PubMed](#)]
142. Beaudouin, J.; Gerlich, D.; Daigle, N.; Eils, R.; Ellenberg, J. Nuclear envelope breakdown proceeds by microtubule-induced tearing of the lamina. *Cell* **2002**, *108*, 83–96. [[CrossRef](#)] [[PubMed](#)]
143. Salina, D.; Bodoor, K.; Eckley, D.M.; Schroer, T.A.; Rattner, J.B.; Burke, B. Cytoplasmic dynein as a facilitator of nuclear envelope breakdown. *Cell* **2002**, *108*, 97–107. [[CrossRef](#)] [[PubMed](#)]
144. Raaijmakers, J.A.; Tanenbaum, M.E.; Medema, R.H. Systematic dissection of dynein regulators in mitosis. *J. Cell Biol.* **2013**, *201*, 201–215. [[CrossRef](#)] [[PubMed](#)]
145. Puhka, M.; Vihinen, H.; Joensuu, M.; Jokitalo, E. Endoplasmic reticulum remains continuous and undergoes sheet-to-tubule transformation during cell division in mammalian cells. *J. Cell Biol.* **2007**, *179*, 895–909. [[CrossRef](#)] [[PubMed](#)]
146. Lu, L.; Ladinsky, M.S.; Kirchhausen, T. Cisternal organization of the endoplasmic reticulum during mitosis. *Mol. Biol. Cell* **2009**, *20*, 3471–3480. [[CrossRef](#)] [[PubMed](#)]
147. Puhka, M.; Joensuu, M.; Vihinen, H.; Belevich, I.; Jokitalo, E. Progressive sheet-to-tubule transformation is a general mechanism for endoplasmic reticulum partitioning in dividing mammalian cells. *Mol. Biol. Cell* **2012**, *23*, 2424–2432. [[CrossRef](#)] [[PubMed](#)]
148. Yang, L.; Guan, T.; Gerace, L. Integral membrane proteins of the nuclear envelope are dispersed throughout the endoplasmic reticulum during mitosis. *J. Cell Biol.* **1997**, *137*, 1199–1210. [[CrossRef](#)] [[PubMed](#)]
149. Hirano, Y.; Segawa, M.; Ouchi, F.S.; Yamakawa, Y.; Furukawa, K.; Takeyasu, K.; Horigome, T. Dissociation of emerin from barrier-to-autointegration factor is regulated through mitotic phosphorylation of emerin in a xenopus egg cell-free system. *J. Biol. Chem.* **2005**, *280*, 39925–39933. [[CrossRef](#)]
150. Hirano, Y.; Iwase, Y.; Ishii, K.; Kumeta, M.; Horigome, T.; Takeyasu, K. Cell cycle-dependent phosphorylation of MAN1. *Biochemistry* **2009**, *48*, 1636–1643. [[CrossRef](#)]
151. Patel, J.T.; Bottrill, A.; Prosser, S.L.; Jayaraman, S.; Straatman, K.; Fry, A.M.; Shackleton, S. Mitotic phosphorylation of SUN1 loosens its connection with the nuclear lamina while the LINC complex remains intact. *Nucleus* **2014**, *5*, 462–473. [[CrossRef](#)]
152. Marcelot, A.; Petitalot, A.; Ropars, V.; Le Du, M.H.; Samson, C.; Dubois, S.; Hoffmann, G.; Miron, S.; Cuniassé, P.; Marquez, J.A.; et al. Di-phosphorylated BAF shows altered structural dynamics and binding to DNA, but interacts with its nuclear envelope partners. *Nucleic Acids Res.* **2021**, *49*, 3841–3855. [[CrossRef](#)] [[PubMed](#)]
153. Deolal, P.; Scholz, J.; Ren, K.; Bragulat-Teixidor, H.; Otsuka, S. Sculpting nuclear envelope identity from the endoplasmic reticulum during the cell cycle. *Nucleus* **2024**, *15*, 2299632. [[CrossRef](#)] [[PubMed](#)]
154. Bengtsson, L.; Wilson, K.L. Barrier-to-autointegration factor phosphorylation on Ser-4 regulates emerin binding to lamin A in vitro and emerin localization in vivo. *Mol. Biol. Cell* **2006**, *17*, 1154–1163. [[CrossRef](#)]
155. Molitor, T.P.; Traktman, P. Depletion of the protein kinase VRK1 disrupts nuclear envelope morphology and leads to BAF retention on mitotic chromosomes. *Mol. Biol. Cell* **2014**, *25*, 891–903. [[CrossRef](#)] [[PubMed](#)]
156. Fernandez-Alvarez, A.; Cooper, J.P. Chromosomes Orchestrate Their Own Liberation: Nuclear Envelope Disassembly. *Trends Cell Biol.* **2017**, *27*, 255–265. [[CrossRef](#)] [[PubMed](#)]
157. Pieper, G.H.; Sprenger, S.; Teis, D.; Oliferenko, S. ESCRT-III/Vps4 Controls Heterochromatin-Nuclear Envelope Attachments. *Dev. Cell* **2020**, *53*, 27–41.e6. [[CrossRef](#)] [[PubMed](#)]
158. Dabauvalle, M.C.; Muller, E.; Ewald, A.; Kress, W.; Krohne, G.; Muller, C.R. Distribution of emerin during the cell cycle. *Eur. J. Cell Biol.* **1999**, *78*, 749–756. [[CrossRef](#)]
159. Haraguchi, T.; Koujin, T.; Hayakawa, T.; Kaneda, T.; Tsutsumi, C.; Imamoto, N.; Akazawa, C.; Sukegawa, J.; Yoneda, Y.; Hiraoka, Y. Live fluorescence imaging reveals early recruitment of emerin, LBR, RanBP2, and Nup153 to reforming functional nuclear envelopes. *J. Cell Sci.* **2000**, *113 Pt 5*, 779–794. [[CrossRef](#)]
160. Dechat, T.; Gajewski, A.; Korbei, B.; Gerlich, D.; Daigle, N.; Haraguchi, T.; Furukawa, K.; Ellenberg, J.; Foisner, R. LAP2 $\alpha$  and BAF transiently localize to telomeres and specific regions on chromatin during nuclear assembly. *J. Cell Sci.* **2004**, *117*, 6117–6128. [[CrossRef](#)]
161. Haraguchi, T.; Kojidani, T.; Koujin, T.; Shimi, T.; Osakada, H.; Mori, C.; Yamamoto, A.; Hiraoka, Y. Live cell imaging and electron microscopy reveal dynamic processes of BAF-directed nuclear envelope assembly. *J. Cell Sci.* **2008**, *121*, 2540–2554. [[CrossRef](#)] [[PubMed](#)]

162. Crabbe, L.; Cesare, A.J.; Kasuboski, J.M.; Fitzpatrick, J.A.; Karlseder, J. Human telomeres are tethered to the nuclear envelope during postmitotic nuclear assembly. *Cell Rep.* **2012**, *2*, 1521–1529. [[CrossRef](#)] [[PubMed](#)]
163. Keller, D.; Stinus, S.; Umlauf, D.; Gourbeyre, E.; Biot, E.; Olivier, N.; Mahou, P.; Beaurepaire, E.; Andrey, P.; Crabbe, L. Non-random spatial organization of telomeres varies during the cell cycle and requires LAP2 and BAF. *iScience* **2024**, *27*, 109343. [[CrossRef](#)] [[PubMed](#)]
164. Arii, J.; Watanabe, M.; Maeda, F.; Tokai-Nishizumi, N.; Chihara, T.; Miura, M.; Maruzuru, Y.; Koyanagi, N.; Kato, A.; Kawaguchi, Y. ESCRT-III mediates budding across the inner nuclear membrane and regulates its integrity. *Nat. Commun.* **2018**, *9*, 3379. [[CrossRef](#)] [[PubMed](#)]
165. Ventimiglia, L.N.; Cuesta-Geijo, M.A.; Martinelli, N.; Caballe, A.; Macheboeuf, P.; Miguet, N.; Parnham, I.M.; Olmos, Y.; Carlton, J.G.; Weissenhorn, W.; et al. CC2D1B Coordinates ESCRT-III Activity during the Mitotic Reformation of the Nuclear Envelope. *Dev. Cell* **2018**, *47*, 547–563.e6. [[CrossRef](#)] [[PubMed](#)]
166. Burla, R.; La Torre, M.; Maccaroni, K.; Verni, F.; Giunta, S.; Saggio, I. Interplay of the nuclear envelope with chromatin in physiology and pathology. *Nucleus* **2020**, *11*, 205–218. [[CrossRef](#)] [[PubMed](#)]
167. Gatta, A.T.; Olmos, Y.; Stoten, C.L.; Chen, Q.; Rosenthal, P.B.; Carlton, J.G. CDK1 controls CHMP7-dependent nuclear envelope reformation. *eLife* **2021**, *10*, e59999. [[CrossRef](#)]
168. Kelley, M.E.; Carlini, L.; Kornakov, N.; Aher, A.; Khodjakov, A.; Kapoor, T.M. Spastin regulates anaphase chromosome separation distance and microtubule-containing nuclear tunnels. *Mol. Biol. Cell* **2024**, *35*, ar48. [[CrossRef](#)] [[PubMed](#)]
169. von Appen, A.; LaJoie, D.; Johnson, I.E.; Trnka, M.J.; Pick, S.M.; Burlingame, A.L.; Ullman, K.S.; Frost, A. LEM2 phase separation promotes ESCRT-mediated nuclear envelope reformation. *Nature* **2020**, *582*, 115–118. [[CrossRef](#)]
170. Samwer, M.; Schneider, M.W.G.; Hoefler, R.; Schmalhorst, P.S.; Jude, J.G.; Zuber, J.; Gerlich, D.W. DNA Cross-Bridging Shapes a Single Nucleus from a Set of Mitotic Chromosomes. *Cell* **2017**, *170*, 956–972.e23. [[CrossRef](#)]
171. Penfield, L.; Shankar, R.; Szentgyorgyi, E.; Laffitte, A.; Mauro, M.S.; Audhya, A.; Muller-Reichert, T.; Bahmanyar, S. Regulated lipid synthesis and LEM2/CHMP7 jointly control nuclear envelope closure. *J. Cell Biol.* **2020**, *219*, e201908179. [[CrossRef](#)]
172. Maccaroni, K.; La Torre, M.; Burla, R.; Saggio, I. Phase Separation in the Nucleus and at the Nuclear Periphery during Post-Mitotic Nuclear Envelope Reformation. *Cells* **2022**, *11*, 1749. [[CrossRef](#)]
173. De Vos, W.H.; Houben, F.; Kamps, M.; Malhas, A.; Verheyen, F.; Cox, J.; Manders, E.M.; Verstraeten, V.L.; van Steensel, M.A.; Marcelis, C.L.; et al. Repetitive disruptions of the nuclear envelope invoke temporary loss of cellular compartmentalization in laminopathies. *Hum. Mol. Genet.* **2011**, *20*, 4175–4186. [[CrossRef](#)]
174. Vargas, J.D.; Hatch, E.M.; Anderson, D.J.; Hetzer, M.W. Transient nuclear envelope rupturing during interphase in human cancer cells. *Nucleus* **2012**, *3*, 88–100. [[CrossRef](#)]
175. Ventimiglia, L.N.; Martin-Serrano, J. ESCRT machinery: Damage control at the nuclear membrane. *Cell Res.* **2016**, *26*, 641–642. [[CrossRef](#)]
176. Wallis, S.S.; Ventimiglia, L.N.; Otigbah, E.; Infante, E.; Cuesta-Geijo, M.A.; Kidiyoor, G.R.; Carbajal, M.A.; Fleck, R.A.; Foiani, M.; Garcia-Manyes, S.; et al. The ESCRT machinery counteracts Nesprin-2G-mediated mechanical forces during nuclear envelope repair. *Dev. Cell* **2021**, *56*, 3192–3202.e8. [[CrossRef](#)]
177. Halfmann, C.T.; Sears, R.M.; Katiyar, A.; Busselman, B.W.; Aman, L.K.; Zhang, Q.; O'Bryan, C.S.; Angelini, T.E.; Lele, T.P.; Roux, K.J. Repair of nuclear ruptures requires barrier-to-autointegration factor. *J. Cell Biol.* **2019**, *218*, 2136–2149. [[CrossRef](#)]
178. Liu, S.; Kwon, M.; Mannino, M.; Yang, N.; Renda, F.; Khodjakov, A.; Pellman, D. Nuclear envelope assembly defects link mitotic errors to chromothripsis. *Nature* **2018**, *561*, 551–555. [[CrossRef](#)]
179. Vietri, M.; Schultz, S.W.; Bellanger, A.; Jones, C.M.; Petersen, L.I.; Raiborg, C.; Skarpen, E.; Pedurupillay, C.R.J.; Kjos, I.; Kip, E.; et al. Unrestrained ESCRT-III drives micronuclear catastrophe and chromosome fragmentation. *Nat. Cell Biol.* **2020**, *22*, 856–867. [[CrossRef](#)]
180. Willan, J.; Cleasby, A.J.; Flores-Rodriguez, N.; Stefani, F.; Rinaldo, C.; Pisciottoni, A.; Grant, E.; Woodman, P.; Bryant, H.E.; Ciani, B. ESCRT-III is necessary for the integrity of the nuclear envelope in micronuclei but is aberrant at ruptured micronuclear envelopes generating damage. *Oncogenesis* **2019**, *8*, 29. [[CrossRef](#)]
181. Strzyz, P. ESCRTing membrane collapse. *Nat. Rev. Mol. Cell Biol.* **2020**, *21*, 498–499. [[CrossRef](#)]
182. Warecki, B.; Ling, X.; Bast, I.; Sullivan, W. ESCRT-III-mediated membrane fusion drives chromosome fragments through nuclear envelope channels. *J. Cell Biol.* **2020**, *219*, e201905091. [[CrossRef](#)]
183. Liu, S.; Pellman, D. The coordination of nuclear envelope assembly and chromosome segregation in metazoans. *Nucleus* **2020**, *11*, 35–52. [[CrossRef](#)]
184. Shankar, R.; Lettman, M.M.; Whisler, W.; Frankel, E.B.; Audhya, A. The ESCRT machinery directs quality control over inner nuclear membrane architecture. *Cell Rep.* **2022**, *38*, 110263. [[CrossRef](#)]
185. Mammel, A.E.; Hatch, E.M. Genome instability from nuclear catastrophe and DNA damage. *Semin. Cell Dev. Biol.* **2022**, *123*, 131–139. [[CrossRef](#)]
186. Zeng, Y.; Zhuang, Y.; Vinod, B.; Guo, X.; Mitra, A.; Chen, P.; Saggio, I.; Shivashankar, G.V.; Gao, W.; Zhao, W. Guiding Irregular Nuclear Morphology on Nanopillar Arrays for Malignancy Differentiation in Tumor Cells. *Nano Lett.* **2022**, *22*, 7724–7733. [[CrossRef](#)]
187. Arii, J.; Maeda, F.; Maruzuru, Y.; Koyanagi, N.; Kato, A.; Mori, Y.; Kawaguchi, Y. ESCRT-III controls nuclear envelope deformation induced by progerin. *Sci. Rep.* **2020**, *10*, 18877. [[CrossRef](#)]



188. Isermann, P.; Lammerding, J. Consequences of a tight squeeze: Nuclear envelope rupture and repair. *Nucleus* **2017**, *8*, 268–274. [[CrossRef](#)]
189. Gauthier, B.R.; Lorenzo, P.I.; Comaills, V. Physical Forces and Transient Nuclear Envelope Rupture during Metastasis: The Key for Success? *Cancers* **2022**, *14*, 83. [[CrossRef](#)]
190. Bhutta, M.S.; McNerny, C.J.; Gould, G.W. ESCRT function in cytokinesis: Location, dynamics and regulation by mitotic kinases. *Int. J. Mol. Sci.* **2014**, *15*, 21723–21739. [[CrossRef](#)]
191. Zhao, W.M.; Seki, A.; Fang, G. Cep55, a microtubule-bundling protein, associates with centralspindlin to control the midbody integrity and cell abscission during cytokinesis. *Mol. Biol. Cell* **2006**, *17*, 3881–3896. [[CrossRef](#)] [[PubMed](#)]
192. Bastos, R.N.; Barr, F.A. Plk1 negatively regulates Cep55 recruitment to the midbody to ensure orderly abscission. *J. Cell Biol.* **2010**, *191*, 751–760. [[CrossRef](#)] [[PubMed](#)]
193. Lee, H.H.; Elia, N.; Ghirlando, R.; Lippincott-Schwartz, J.; Hurley, J.H. Midbody targeting of the ESCRT machinery by a noncanonical coiled coil in CEP55. *Science* **2008**, *322*, 576–580. [[CrossRef](#)]
194. Karasmanis, E.P.; Hwang, D.; Nakos, K.; Bowen, J.R.; Angelis, D.; Spiliotis, E.T. A Septin Double Ring Controls the Spatiotemporal Organization of the ESCRT Machinery in Cytokinetic Abscission. *Curr. Biol.* **2019**, *29*, 2174–2182.e7. [[CrossRef](#)]
195. Tedeschi, A.; Almagro, J.; Renshaw, M.J.; Messal, H.A.; Behrens, A.; Petronczki, M. Cep55 promotes cytokinesis of neural progenitors but is dispensable for most mammalian cell divisions. *Nat. Commun.* **2020**, *11*, 1746. [[CrossRef](#)]
196. Elia, N.; Sougrat, R.; Spurlin, T.A.; Hurley, J.H.; Lippincott-Schwartz, J. Dynamics of endosomal sorting complex required for transport (ESCRT) machinery during cytokinesis and its role in abscission. *Proc. Natl. Acad. Sci. USA* **2011**, *108*, 4846–4851. [[CrossRef](#)]
197. Gershony, O.; Sherman, S.; Adar, S.; Segal, I.; Nachmias, D.; Goliand, I.; Elia, N. Measuring abscission spatiotemporal dynamics using quantitative high-resolution microscopy. *Methods Cell Biol.* **2017**, *137*, 205–224.
198. Sherman, S.; Kirchenbuechler, D.; Nachmias, D.; Tamir, A.; Werner, S.; Elbaum, M.; Elia, N. Resolving new ultrastructural features of cytokinetic abscission with soft-X-ray cryo-tomography. *Sci. Rep.* **2016**, *6*, 27629. [[CrossRef](#)]
199. Christ, L.; Wenzel, E.M.; Liestol, K.; Raiborg, C.; Campsteijn, C.; Stenmark, H. ALIX and ESCRT-I/II function as parallel ESCRT-III recruiters in cytokinetic abscission. *J. Cell Biol.* **2016**, *212*, 499–513. [[CrossRef](#)]
200. Goliand, I.; Adar-Levor, S.; Segal, I.; Nachmias, D.; Dadosh, T.; Kozlov, M.M.; Elia, N. Resolving ESCRT-III Spirals at the Intercellular Bridge of Dividing Cells Using 3D STORM. *Cell Rep.* **2018**, *24*, 1756–1764. [[CrossRef](#)]
201. Agromayor, M.; Carlton, J.G.; Phelan, J.P.; Matthews, D.R.; Carlin, L.M.; Ameer-Beg, S.; Bowers, K.; Martin-Serrano, J. Essential role of hist1 in cytokinesis. *Mol. Biol. Cell* **2009**, *20*, 1374–1387. [[CrossRef](#)]
202. Guizetti, J.; Schermelleh, L.; Mantler, J.; Maar, S.; Poser, I.; Leonhardt, H.; Muller-Reichert, T.; Gerlich, D.W. Cortical constriction during abscission involves helices of ESCRT-III-dependent filaments. *Science* **2011**, *331*, 1616–1620. [[CrossRef](#)]
203. Schoneberg, J.; Pavlin, M.R.; Yan, S.; Righini, M.; Lee, I.H.; Carlson, L.A.; Bahrami, A.H.; Goldman, D.H.; Ren, X.; Hummer, G.; et al. ATP-dependent force generation and membrane scission by ESCRT-III and Vps4. *Science* **2018**, *362*, 1423–1428. [[CrossRef](#)]
204. Connell, J.W.; Lindon, C.; Luzio, J.P.; Reid, E. Spastin couples microtubule severing to membrane traffic in completion of cytokinesis and secretion. *Traffic* **2009**, *10*, 42–56. [[CrossRef](#)]
205. Steigemann, P.; Gerlich, D.W. An evolutionary conserved checkpoint controls abscission timing. *Cell Cycle* **2009**, *8*, 1814–1815. [[CrossRef](#)]
206. Petsalaki, E.; Zachos, G. The Abscission Checkpoint: A Guardian of Chromosomal Stability. *Cells* **2021**, *10*, 3350. [[CrossRef](#)]
207. Norden, C.; Mendoza, M.; Dobbelaere, J.; Kotwaliwale, C.V.; Biggins, S.; Barral, Y. The NoCut pathway links completion of cytokinesis to spindle midzone function to prevent chromosome breakage. *Cell* **2006**, *125*, 85–98. [[CrossRef](#)] [[PubMed](#)]
208. Mendoza, M.; Norden, C.; Durrer, K.; Rauter, H.; Uhlmann, F.; Barral, Y. A mechanism for chromosome segregation sensing by the NoCut checkpoint. *Nat. Cell Biol.* **2009**, *11*, 477–483. [[CrossRef](#)]
209. Steigemann, P.; Wurzenberger, C.; Schmitz, M.H.; Held, M.; Guizetti, J.; Maar, S.; Gerlich, D.W. Aurora B-mediated abscission checkpoint protects against tetraploidization. *Cell* **2009**, *136*, 473–484. [[CrossRef](#)]
210. Petsalaki, E.; Zachos, G. Clks 1, 2 and 4 prevent chromatin breakage by regulating the Aurora B-dependent abscission checkpoint. *Nat. Commun.* **2016**, *7*, 11451. [[CrossRef](#)]
211. Carlton, J.G.; Caballe, A.; Agromayor, M.; Kloc, M.; Martin-Serrano, J. ESCRT-III governs the Aurora B-mediated abscission checkpoint through CHMP4C. *Science* **2012**, *336*, 220–225. [[CrossRef](#)]
212. McCullough, J.; Fisher, R.D.; Whitby, F.G.; Sundquist, W.I.; Hill, C.P. ALIX-CHMP4 interactions in the human ESCRT pathway. *Proc. Natl. Acad. Sci. USA* **2008**, *105*, 7687–7691. [[CrossRef](#)]
213. Thoresen, S.B.; Campsteijn, C.; Vietri, M.; Schink, K.O.; Liestol, K.; Andersen, J.S.; Raiborg, C.; Stenmark, H. ANCHR mediates Aurora-B-dependent abscission checkpoint control through retention of VPS4. *Nat. Cell Biol.* **2014**, *16*, 550–560. [[CrossRef](#)]
214. Pike, T.; Brownlow, N.; Kjaer, S.; Carlton, J.; Parker, P.J. PKCvarepsilon switches Aurora B specificity to exit the abscission checkpoint. *Nat. Commun.* **2016**, *7*, 13853. [[CrossRef](#)]
215. Petsalaki, E.; Balafouti, S.; Kyriazi, A.A.; Zachos, G. The abscission checkpoint senses chromatin bridges through Top2 $\alpha$  recruitment to DNA knots. *J. Cell Biol.* **2023**, *222*, e202303123. [[CrossRef](#)]
216. Amaral, N.; Vendrell, A.; Funaya, C.; Idrissi, F.Z.; Maier, M.; Kumar, A.; Neurohr, G.; Colomina, N.; Torres-Rosell, J.; Geli, M.I.; et al. The Aurora-B-dependent NoCut checkpoint prevents damage of anaphase bridges after DNA replication stress. *Nat. Cell Biol.* **2016**, *18*, 516–526. [[CrossRef](#)]

217. Chan, K.L.; Palmari-Pallag, T.; Ying, S.; Hickson, I.D. Replication stress induces sister-chromatid bridging at fragile site loci in mitosis. *Nat. Cell Biol.* **2009**, *11*, 753–760. [[CrossRef](#)]
218. Wilhelm, T.; Magdalou, I.; Barascu, A.; Techer, H.; Debatisse, M.; Lopez, B.S. Spontaneous slow replication fork progression elicits mitosis alterations in homologous recombination-deficient mammalian cells. *Proc. Natl. Acad. Sci. USA* **2014**, *111*, 763–768. [[CrossRef](#)]
219. Maciejowski, J.; Li, Y.; Bosco, N.; Campbell, P.J.; de Lange, T. Chromothripsis and Kataegis Induced by Telomere Crisis. *Cell* **2015**, *163*, 1641–1654. [[CrossRef](#)]
220. West, S.C.; Chan, Y.W. Genome Instability as a Consequence of Defects in the Resolution of Recombination Intermediates. *Cold Spring Harb. Symp. Quant. Biol.* **2017**, *82*, 207–212. [[CrossRef](#)]
221. Chanboonyasitt, P.; Chan, Y.W. Regulation of mitotic chromosome architecture and resolution of ultrafine anaphase bridges by PICH. *Cell Cycle* **2021**, *20*, 2077–2090. [[CrossRef](#)] [[PubMed](#)]
222. Liu, Y.; Nielsen, C.F.; Yao, Q.; Hickson, I.D. The origins and processing of ultra fine anaphase DNA bridges. *Curr. Opin. Genet. Dev.* **2014**, *26*, 1–5. [[CrossRef](#)] [[PubMed](#)]
223. Petsalaki, E.; Zachos, G. An ATM-Chk2-INCENP pathway activates the abscission checkpoint. *J. Cell Biol.* **2021**, *220*, e202008029. [[CrossRef](#)]
224. Bhowmick, R.; Thakur, R.S.; Venegas, A.B.; Liu, Y.; Nilsson, J.; Barisic, M.; Hickson, I.D. The RIF1-PP1 Axis Controls Abscission Timing in Human Cells. *Curr. Biol.* **2019**, *29*, 1232–1242.e5. [[CrossRef](#)]
225. Watson, L.; Soliman, T.N.; Davis, K.; Kelly, J.; Lockwood, N.; Yang, X.; Lynham, S.; Scott, J.D.; Crossland, V.; McDonald, N.Q.; et al. Co-ordinated control of the Aurora B abscission checkpoint by PKCepsilon complex assembly, midbody recruitment and retention. *Biochem. J.* **2021**, *478*, 2247–2263. [[CrossRef](#)]
226. Caballe, A.; Wenzel, D.M.; Agromayor, M.; Alam, S.L.; Skalicky, J.J.; Kloc, M.; Carlton, J.G.; Labrador, L.; Sundquist, W.I.; Martin-Serrano, J. ULK3 regulates cytokinetic abscission by phosphorylating ESCRT-III proteins. *eLife* **2015**, *4*, e06547. [[CrossRef](#)]
227. Dandoulaki, M.; Petsalaki, E.; Sumpton, D.; Zanivan, S.; Zachos, G. Src activation by Chk1 promotes actin patch formation and prevents chromatin bridge breakage in cytokinesis. *J. Cell Biol.* **2018**, *217*, 3071–3089. [[CrossRef](#)] [[PubMed](#)]
228. Fletcher, D.A.; Mullins, R.D. Cell mechanics and the cytoskeleton. *Nature* **2010**, *463*, 485–492. [[CrossRef](#)]
229. Bai, J.; Wioland, H.; Advedissian, T.; Cuvelier, F.; Romet-Lemonne, G.; Echard, A. Actin reduction by MsrB2 is a key component of the cytokinetic abscission checkpoint and prevents tetraploidy. *Proc. Natl. Acad. Sci. USA* **2020**, *117*, 4169–4179. [[CrossRef](#)]
230. Strohacker, L.K.; Mackay, D.R.; Whitney, M.A.; Couldwell, G.C.; Sundquist, W.I.; Ullman, K.S. Identification of abscission checkpoint bodies as structures that regulate ESCRT factors to control abscission timing. *eLife* **2021**, *10*, e63743. [[CrossRef](#)] [[PubMed](#)]
231. Umbreit, N.T.; Zhang, C.Z.; Lynch, L.D.; Blaine, L.J.; Cheng, A.M.; Tourdot, R.; Sun, L.; Almubarak, H.F.; Judge, K.; Mitchell, T.J.; et al. Mechanisms generating cancer genome complexity from a single cell division error. *Science* **2020**, *368*, eaba0712. [[CrossRef](#)] [[PubMed](#)]
232. Crasta, K.; Ganem, N.J.; Dagher, R.; Lantermann, A.B.; Ivanova, E.V.; Pan, Y.; Nezi, L.; Protopopov, A.; Chowdhury, D.; Pellman, D. DNA breaks and chromosome pulverization from errors in mitosis. *Nature* **2012**, *482*, 53–58. [[CrossRef](#)]
233. Stephens, P.J.; Greenman, C.D.; Fu, B.; Yang, F.; Bignell, G.R.; Mudie, L.J.; Pleasance, E.D.; Lau, K.W.; Beare, D.; Stebbings, L.A.; et al. Massive genomic rearrangement acquired in a single catastrophic event during cancer development. *Cell* **2011**, *144*, 27–40. [[CrossRef](#)] [[PubMed](#)]
234. Fujiwara, T.; Bandi, M.; Nitta, M.; Ivanova, E.V.; Bronson, R.T.; Pellman, D. Cytokinesis failure generating tetraploids promotes tumorigenesis in p53-null cells. *Nature* **2005**, *437*, 1043–1047. [[CrossRef](#)]
235. Gisselsson, D.; Pettersson, L.; Hoglund, M.; Heidenblad, M.; Gorunova, L.; Wiegant, J.; Mertens, F.; Dal Cin, P.; Mitelman, F.; Mandahl, N. Chromosomal breakage-fusion-bridge events cause genetic intratumor heterogeneity. *Proc. Natl. Acad. Sci. USA* **2000**, *97*, 5357–5362. [[CrossRef](#)]
236. Maciejowski, J.; Chatzipli, A.; Dananberg, A.; Chu, K.; Toufektchan, E.; Klimczak, L.J.; Gordenin, D.A.; Campbell, P.J.; de Lange, T. APOBEC3-dependent kataegis and TREX1-driven chromothripsis during telomere crisis. *Nat. Genet.* **2020**, *52*, 884–890. [[CrossRef](#)]
237. Hatch, E.M.; Fischer, A.H.; Deerinck, T.J.; Hetzer, M.W. Catastrophic nuclear envelope collapse in cancer cell micronuclei. *Cell* **2013**, *154*, 47–60. [[CrossRef](#)] [[PubMed](#)]
238. Zhang, C.Z.; Spektor, A.; Cornils, H.; Francis, J.M.; Jackson, E.K.; Liu, S.; Meyerson, M.; Pellman, D. Chromothripsis from DNA damage in micronuclei. *Nature* **2015**, *522*, 179–184. [[CrossRef](#)]
239. Jiang, H.; Chan, Y.W. Chromatin bridges: Stochastic breakage or regulated resolution? *Trends Genet.* **2024**, *40*, 69–82. [[CrossRef](#)]
240. Bach, D.H.; Zhang, W.; Sood, A.K. Chromosomal Instability in Tumor Initiation and Development. *Cancer Res.* **2019**, *79*, 3995–4002. [[CrossRef](#)]
241. Lens, S.M.A.; Medema, R.H. Cytokinesis defects and cancer. *Nat. Rev. Cancer* **2019**, *19*, 32–45. [[CrossRef](#)] [[PubMed](#)]
242. Cortes-Ciriano, I.; Lee, J.J.; Xi, R.; Jain, D.; Jung, Y.L.; Yang, L.; Gordenin, D.; Klimczak, L.J.; Zhang, C.Z.; Pellman, D.S.; et al. Comprehensive analysis of chromothripsis in 2,658 human cancers using whole-genome sequencing. *Nat. Genet.* **2020**, *52*, 331–341. [[CrossRef](#)] [[PubMed](#)]
243. Chieffi, P. Aurora B: A new promising therapeutic target in cancer. *Intractable Rare Dis. Res.* **2018**, *7*, 141–144. [[CrossRef](#)] [[PubMed](#)]
244. Chen, Y.J.; Chen, C.M.; Twu, N.F.; Yen, M.S.; Lai, C.R.; Wu, H.H.; Wang, P.H.; Yuan, C.C. Overexpression of Aurora B is associated with poor prognosis in epithelial ovarian cancer patients. *Virchows Arch.* **2009**, *455*, 431–440. [[CrossRef](#)] [[PubMed](#)]

245. Lopez-Rios, F.; Chuai, S.; Flores, R.; Shimizu, S.; Ohno, T.; Wakahara, K.; Illei, P.B.; Hussain, S.; Krug, L.; Zakowski, M.F.; et al. Global gene expression profiling of pleural mesotheliomas: Overexpression of aurora kinases and P16/CDKN2A deletion as prognostic factors and critical evaluation of microarray-based prognostic prediction. *Cancer Res.* **2006**, *66*, 2970–2979. [[CrossRef](#)] [[PubMed](#)]
246. Sadler, J.B.A.; Wenzel, D.M.; Strohacker, L.K.; Guindo-Martinez, M.; Alam, S.L.; Mercader, J.M.; Torrents, D.; Ullman, K.S.; Sundquist, W.I.; Martin-Serrano, J. A cancer-associated polymorphism in ESCRT-III disrupts the abscission checkpoint and promotes genome instability. *Proc. Natl. Acad. Sci. USA* **2018**, *115*, E8900–E8908. [[CrossRef](#)] [[PubMed](#)]
247. Pharoah, P.D.; Tsai, Y.Y.; Ramus, S.J.; Phelan, C.M.; Goode, E.L.; Lawrenson, K.; Buckley, M.; Fridley, B.L.; Tyrer, J.P.; Shen, H.; et al. GWAS meta-analysis and replication identifies three new susceptibility loci for ovarian cancer. *Nat. Genet.* **2013**, *45*, 362–370. [[CrossRef](#)]
248. Szymanska, E.; Nowak, P.; Kolmus, K.; Cybulska, M.; Goryca, K.; Derezińska-Wolek, E.; Szumera-Cieckiewicz, A.; Brewinska-Olchowik, M.; Grochowska, A.; Piwocka, K.; et al. Synthetic lethality between VPS4A and VPS4B triggers an inflammatory response in colorectal cancer. *EMBO Mol. Med.* **2020**, *12*, e10812. [[CrossRef](#)]
249. Neggers, J.E.; Paoletta, B.R.; Asfaw, A.; Rothberg, M.V.; Skipper, T.A.; Yang, A.; Kalekar, R.L.; Krill-Burger, J.M.; Dharia, N.V.; Kugener, G.; et al. Synthetic Lethal Interaction between the ESCRT Paralog Enzymes VPS4A and VPS4B in Cancers Harboring Loss of Chromosome 18q or 16q. *Cell Rep.* **2020**, *33*, 108493. [[CrossRef](#)]

**Disclaimer/Publisher’s Note:** The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.