A novel role of lamins from genetic disease to cancer biomarkers

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Abstract

Lamins are the key components of the nuclear lamina and by virtue of their interactions with chromatin and binding partners act as regulators of cell proliferation and differentiation. Of late, the diverse roles of lamins in cellular processes have made them the topic of intense debate for their role in cancer progression. The observations about aberrant localization or misexpression of the nuclear lamins in cancerous tissues have often led to the speculative role of lamins as a cancer risk biomarker. Here we discuss the involvement of lamins in several cancer subtypes and their potential role in predicting the tumor progression.

Introduction

The animal cell nuclei have a characteristic feature of a well-defined nuclear architecture and chromatin compartmentalization. The complex nuclear organization has been attributed to the increase in genome complexity and need for spatiotemporal regulation of the gene expression in higher vertebrates. Typical metazoan nucleus has been identified into three principal components- nuclear pore complex (NPC), nucleoplasm and lamina. The lamina is the meshwork of proteins found on the nucleoplasmic face of the inner nuclear membrane. A family of type V intermediate filaments (IF) proteins called lamins is the principal component of this lamina. This family of proteins is found among all metazoans except Hydra and arthropods, and is localized exclusively in the nucleus unlike other members of intermediate filaments family.1 Absence of lamins or their homologs in plants and yeast support the notion that these proteins have evolved during the transition from open to closed mitosis.2 However, recent studies show that plants have a substitute for lamin proteins. Even though the lamin-like proteins does not show sequence similarity, their secondary structure, nuclear distribution, their influence in nuclear shape and size suggests them as functional lamin analogs.3 In addition, homologs of metazoan lamins and lamin gene tree support the vertical evolution of lamin from the last eukaryotic common ancestor.4

As we move higher on the evolutionary scale, the number and complexity of lamin isoforms increases from single \textit{lmn-1} of \textit{C. elegans} to two (Dm0 and lamC) in Drosophila to three (LMNB1, LMNB2, and LMNA) in human.5,6 The evolutionarily conserved lamins are subdivided into A- and B-type based on their biochemical properties, and for its conserved expression from worms to human, lamin B is considered as evolutionary precursor of lamin A. Among the lamin subtypes, B-type lamins have a ubiquitous expression and are considered essential for cell survival. A-type lamins, however, show a spatiotemporal expression during development and are majorly expressed in all differentiated cells and in some adult stem cells, while being considered absent in embryonic stem cells.7,8 Lamin A and lamin C (collectively referred as lamin A/C) are alternative splice variants of the \textit{LMNA} gene while lamin B1 and lamin B2 are transcribed from \textit{LMNB1} and \textit{LMNB2} respectively. Several studies have shown tissue-restricted expression of \textit{LMNA}, minor splice variants lamin A10, lamin C2, and also for lamin B3 a splice variant of \textit{LMNB2}, indicating the specialized roles of these proteins.8 Lamins C2 and B3 are shown to be germ-cell specific whereas lamin A10 has been detected in cell lines derived from colon, lung, and breast carcinomas.

Lamins are known to be the major building blocks of nuclear structure, its shape, and provide mechanical steadiness to the cell nucleus by protecting them from mechanical forces especially in load bearing cells like muscles. They also directly or indirectly regulate gene expression, differentiation, DNA repair, and apoptosis. They bind to chromatin in a sequence independent manner or through their binding partners and are determining factors for chromatin positioning in the nucleus.10-12 Recently, disease causing A-type lamin mutants have been reported to be involved in regulating proteolytic degradation of proteins, affecting protein stability, and nuclear speckle13 stability. Lamins are known to interact with cytoskeleton through nuclear membrane SUN and KASH domain containing proteins and are crucial for mechanotransduction and mechanical stability of the cell. Studies with lamin A/C deficient embryonic fibroblast have shown impaired mechanotransduction and decreased mechanical stiffness.14

The human \textit{LMNA} gene has 12 exons and studies spanning over two decades have reported more than 300 disease-causing mutations throughout the gene (9). These mutations lead to a wide variety of pleiotropic disorders with varying penetrance, which collectively with B-type lamin-associated diseases, are referred to as laminopathies.15
Depending on mutation involved, the laminopathies can affect a particular type of tissue or may manifest as a complex disorder affecting several tissues. The majority of the laminopathies affect tissues such as muscles, cardiomyocytes, adipocytes, and neurons, which are mesodermal in origin. Loss of binding of mutant lamin A/C to pRb, cyclin D3, and emerin has been attributed to defective myoblast differentiation due to reduction in MyoD, desmin, and M-cadherin, thereby leading to muscle degeneration/dystrophy.9 Two of the most studied laminopathies involving muscle tissues are Emery-Dreifuss muscular dystrophy (EMD) and limb-girdle muscular dystrophy (LGMD-1B). The late onset dilated cardiomyopathy and conduction-system disease (DCM-1A), the Charcot-Marie Tooth disorder, a neuropathy with peripheral nerve involvement (CMT-2B1), the Dunnigan-type familial partial lipodystrophy (FPLD), and the systemic disorders Hutchinson-Gilford progeria (HGPS), mandibuloacral dysplasia (MAD), and restrictive dermopathy (RD) have also been attributed to mutations in A-type laminas or their binding partners. On the other hand, mutations in B-type lamins are usually lethal and hence very rare. The only reported cases are of duplication of LMNB1 leading to adult-onset autosomal dominant leukodystrophy (ADLD), a neurodegenerative disorder characterized by myelin loss in the central nervous system,14 and recently a LMNB1 polymorphic variant was implicated as a modifier of neural tube closure defects.15 Individuals with LMNB2 heterozygous mutations are found to be susceptible to acquired partial lipodystrophy. Despite extensive studies, a comprehensive explanation for tissue restricted phenotype and the mechanism is still elusive.

Lamins and cancer

Many researchers and cancer biologist very well ascribed the relationship between aberrant expression of lamin and cancer subtype by investigating the changes in expression profile of lamin in diverse types of cancers. The improper expression of lamins and its interaction with other proteins are often present in tumor cells. For example, A-type lamins interact with a number of transcription factors and regulates both differentiation and proliferation in cells. Lamin A/C binding regulates emerin, pRb, c-Fos, SREBP1, MOK2 function and plays a role in p53, MAPK, ERK1/2, Wnt, TGF-β, Notch, and NF-kβ signaling. Studies with lamin A mutant overexpression have demonstrated a role for lamin A in myogenesis, adipogenesis, and osteogenesis. Expression of lamin A mutants in adult stem cells shows diminished potential to differentiate and regenerate tissues. Lamin A also regulates gene expression by binding chromatin to the nuclear periphery. Reduced or null expression of A-type lamins often correlates with low levels of differentiation and higher proliferation in cells. Furthermore, loss of lamin A leads to nuclear lobulations and changes in nuclear shape.17-18 Cancer cells are often characterized as highly proliferative with unregulated signaling, having irregular nuclear morphology and properties resembling stem cells.19,20 The diverse functions and wide interactome of lamins have often led to the speculative role of lamins as a cancer risk biomarker that could predict the probability of tumor progression and therefore prognosis. In the following sections we emphasize the involvement of lamins in several cancers subtypes.

Role of lamins in colorectal cancer

Colorectal cancer is the third major type of cancer in both men and women not only in the United States but also worldwide. The aberrant or misexpression of lamins are also present in these type of cancers. A recent investigation provided a comprehensive link between lamin A/C expression, patient prognosis and colorectal cancer (CRC) progression by comparing colorectal cancer and normal colon tissues for lamin expression. Using the Cox proportional hazard ratio (HR) method, patients were observed to have poor prognosis with almost two fold increase in mortality when the tumors tested positive for A-type lamin expression than patients with A-type lamin negative tumours. Lamin A/C expression is majorly deficient from the cells of the colon crypts except for a few basal crypt cells, which are believed to be stem cells. Ectopic expression of GFP-lamin A in colorectal cancer cells revealed increased in cell motility accompanied by an up-regulation of F-plastin, an actin bundling protein, and down regulation of E-cadherin, a protein involved in cell adherence. The study implicates lamin A/C expression as a significant risk indicator of colorectal cancer-related morality, probably due to increase in migratory and stem cell like properties.21

Another investigation revealed a correlation between A-type lamin expression and disease recurrence/clinical outcome of stage II and III colon cancer patients. Using paraffin embedded tissues and tissue microarrays, the authors observed low levels of lamin A/C expression had a greater correlation with high disease recurrence, and suggested that these patients may benefit from adjuvant chemotherapy.22 They also observed that microsatellite stable tumors exhibited more frequently low level of LMNA expression than microsatellite unstable tumors. Moreover, a recent study for role of a calcium binding protein S100A6 and its interacting protein β-catenin, a Wnt pathway effector, in colorectal cancer tissues found that high levels of S100A6 expression is observed in metastatic versus non-metastatic human colorectal cancer cell lines. S100A6 protein was also established as a novel interacting partner of lamin A/C protein, hence potentially linking lamin A/C in colorectal cancer development and progression.23 This clearly indicates that improper regulation of lamins leads to various type of gastrointestinal cancers, in later section of the review we shall discuss other form of gastrointestinal cancers also.

Role of lamins in pancreatic cancer

A recent study designed to look at the mechanism of betulinic acid treatment of pancreatic cancer discovered lamin B1 overexpression in pancreatic cancer. The drug betulinic acid shows antitumor property by down-regulating lamin B1 expression. Lamin B1 overexpression could serve as a biomarker in pancreatic cancer as the study found it to be associated with more malignant form of cancer with poor prognosis of patients.24

Role of lamins in other gastrointestinal cancer

The various intermediate pathological steps of gastrointestinal cancer are easily identifiable, making it easier to observe the changes in expression of nuclear lamins accompanying cancer progression.25 But, there have been a few studies linking expression of nuclear lamins and progression of gastrointestinal cancer. In one such study it was found that in gastrointestinal neoplasm both types of lamins have reduced expression with A-type lamins having a more pronounced effect in case of gastric dysplasia. However, no such reduction was observed in stages of intestinal metaplasia and gastric atrophy. This reduction in expression was accompanied by aberrant, cytoplasmic detection of lamins by immunolabelling. Comparative studies with other solid state tumors showed reduced expression of both lamins- A/C and B1, frequently in squamous and adenocarcinoma of the esophagus, cervical and uterine cancers, breast cancer, and bronchial carcinoma but not in pancreatic
and hepatic cancer. Hence, reduced expression of nuclear lamins may serve as a potential indicator of early stages of gastrointestinal cancer and cytoplasmic detection as an indicator of a more malignant form.26

Role of lamins in neuroblastoma

Lamin A/C shows spatiotemporal expression during development and has a potential role in neurogenesis.8 Neuroblastoma is a solid tumor frequently observed in childhood involving primitive cells of the sympathetic nervous system with an ability to undergo differentiation. A key therapeutic intervention for this aggressive tumor is to induce differentiation by various chemical agents.27 The observation that initial stages of human neuroblastomas show reduced expression of lamin A/C protein in the majority of these cases prompted to study the role of A-type lamins in differentiation and progression of neuroblastoma by knocking down lamin A/C in neuroblastoma cells. Cells with depleted lamin A/C levels fail to undergo retinoic acid-induced differentiation have increased cell migration and drug resistance. The inability to differentiate is further indicated by the absence of distinctive neurites outgrowth and reduced expression of neural markers.28 Collectively, the studies indicate that reduced levels of lamin A/C expression could be used as a diagnostic tool for the more aggressive form of neuroblastoma.

Role of lamins in prostate cancer

A study on progression of various states of prostate cancer by comparing several human prostate cancer cell lines observed a correlation between post-translational modification of B-type lamin and the state of differentiation/proliferation in prostate cancer cells. Although the expression levels of B-type lamins were comparable between the cell lines, the malignant PC3 cells showed an increase in lamin B phosphorylation. As the lamins have been identified as a primary component of nuclear matrix (NM) and Matrix Associated Regions (MARs) the authors speculate that modifying the interactions between NM and MARs may affect gene expression giving rise to a more malignant phenotype.29 These results are supported by an independent study by a different group which reported that knock-down of a nuclear protein McCP2 in PC3 and LNCaP cells causes aberrant proliferation and defective cell cycle progression. This defect is accompanied by diminished lamin A/C, lamin B1 and lamin B receptor (LBR) protein levels and altered nuclear shape.30 Since, MeCP2 interacts with LBR and HP1 to anchor chromatin at the nuclear periphery, its deficit might lead to reduced cell proliferation and viability. Another study involving prostate cancer cell lines observed increase in lamin B-deficient microdomains (LDMDs) and nuclear lobulation, often correlating with augmented aggressiveness and motility of prostate cancer cells. Genes localizing to LDMDs show decreased expression due to stalled Pol II at the promoters in that region. The authors demonstrated that chromosome regions linked to prostate cancer susceptibility mostly localize to LDMDs.31 These observations provide mechanistic insights of B-type lamins in development and progression of prostate cancer.

In another investigation using different prostate cancer cell lines as model for disease progression, found that increased A-type lamin expression leads to increased cell growth, colony formation, and malignancy of prostate cancer cells. It can be argued that increased A type-lamin expression may modulate PI3K/AKT/PTEN signaling pathway by altered mechanotransduction between and nucleus and cytoplasmic membrane and lead to aberrant cell proliferation.32 By using 2D-DIGE and MALDI-TOF/TOF mass spectrometry Skvortsov et al. reported lamin A is a differentially expressed abundant protein between low and high Gleason score prostate tumors. These observations clearly put forward that A-type lamins might serve as a biomarker of tumor differentiation and prognosis and as a novel therapeutic target for prostate cancer.33

Role of lamins in germ cell cancer

Seminoma and non-seminoma are two main types of germ cell tumors that occur in men. They differ in growth rate with non-seminoma having more rapid growth in comparison. Most non-seminoma tumors are of mixed type and the percentage of embryonic carcinoma subtype predicts the malignancy of germ cell tumor.34 In an attempt to study lamin expression in testicular germ cell tumors, cryo-preserved tissue sections of the normal testis and various other testicular germ cell tumors were coimmunostained for both A- and B-type lamins. In testicular germ cell tumors, while B-type lamins were frequently found to be expressed, A-type lamins depicted differential expression with only lamin C being expressed in embryonic carcinoma. This differential expression could help establish detection of embryonic carcinoma in tumors and act as a prognostic marker.35

Role of lamins in liver cancer

Like other cancers Hepatocellular carcinoma (HCC) also involves aberrant gene expression and is frequently observed along with liver cirrhosis. Lamin B1 may be considered as a marker for cirrhosis, because its expression level changes considerably in cirrhotic tissue as compared to normal tissue.36 The expression level of not only Lamin B1 but also both the subtypes of lamins was investigated in hepatocellular regeneration during liver cirrhosis and in different grades of hepatocellular carcinomas. Immunohistochemistry on frozen tissue sections revealed lamin expression both in cirrhosis and carcinomas.37 The proteomic expression profiling and clinicopathological study of diseased and patients suffering from cirrhotic liver and HCC identified lamin B1 and vimentin as predominant proteins elevated in cancerous tissues. Circulating lamin B1 and vimentin could serve as novel biomarkers of early stage HCC that could be detected by noninvasive method.38 Another group performed similar proteomic analysis of normal and cancerous tissue and identified sarcosine dehydrogenase, liver carboxylesterase, peptidyl-prolyl isomerase A, and lamin B1 as novel hepatocellular carcinoma biomarkers.39 Hence, testing for increase in lamin B1 expression could lead to early detection of hepatocellular carcinoma. Thus, Lamin in combination with other liver enzymes that overexpressed in Hepatocellular carcinoma could be a good diagnostic marker.

Role of lamins in lung cancer

The correlation between lamin expression and lung cancer was one of the earliest investigation relating lamins to cancer progression.30 Kaufmann group has shown that the A-type lamins decreased in small cell lung cancer (SCLC) cell lines. They also demonstrated that lamin A/C levels were more than 80% lower in SCLC cell lines compared to non-SCLC lines.30,31 When lamin expression was compared between small cell lung cancer (SCLC), squamous cell carcinomas, and adenocarcinomas it was found that lamin B expression was unaltered, and lamin A/C expression was weaker in SCLC cell lines compared to non-SCLC cell lines.39 Similar results were observed when A and B- type
lamin expression was compared between various non-SCLC and SCLC lines. Expression of v-rasH oncogene in the NCI-H249 small cell line gives rise to phenotype resembling large cell carcinoma of the lung and increase in expression of lamin A/C and vimentin. Here, increase in lamin A/C expression is associated with increased malignancy of lung cancer.48 Another study took a closer look at the protein expression profile of cancer cell line A549 and compared it to normal lung fibroblast cell line MRC-5. Lamin A/C was found to be overexpressed in A549 cells and was postulated to be a biomarker of lung cancer for early detection.41 Studying the expression of A-type lamins in lung adenocarcinoma cell line GLC-A1 showed that not only was the expression of lamin A/C reduced, but also there were significantly higher levels of lamin C compared to lamin A.42 Recent studies with A549 cell lines and green tea polyphenols reported to have antitumor properties showed that green tea extract induced upregulation of lamin A/C expression. The increased A-type lamins in turn can lead to altered actin remodeling and consequently, reduced cell motility. The result is in contradiction to earlier discussed report as authors here show that lamin A/C overexpression seemingly reduces the migratory property of lung cancer cells.43 In most of the lung cancer, B-type lamins are generally overexpressed. Taken together, we can clearly see that Lamin A/C act as diagnostic marker in early stages of lung cancer while Lamin B1 can be a good marker for later stages of cancer.

Role of lamins in breast cancer

Expression patterns of lamin subtypes between normal human skin, actinic keratosis, squamous cell carcinoma (SSC) and basal cell carcinoma (BCC) were correlated to their proliferative potential using immunohistochemistry. Though A and B-type lamins are expressed in both normal and cancerous epidermal cells, a high percentage of proliferating cells found in basal and squamous cell carcinomas stain positive for lamin A expression, suggesting these cells may undergo differentiation.44 Another important oncogene that correlates well with BCC progression is GLI1. A small molecule inhibitor of the hedgehog signaling, Vismodegib has been recently approved by FDA for BCC treatment. While many strategies have been documented to overcome GLI1’s role in cancer,20,45 especially BCC,46 the relationship between lamins and GLI1 has to be elucidated in detail. Another study examined the importance of variation in lamin expression as a diagnostic marker in keratinocytic tumors. The expression of all kinds of lamins was reduced with lamin B showing heterogenous pattern in differentiated SCCs and keratoacanthomas.47 A detailed analysis of lamin subtypes was performed in tissue sections of basal cell carcinomas leading to the categorization of four types of cells lamin A negative, lamin C negative, lamin A/C negative and lamin A/B2 negative. Correlation of these cell subtypes to proliferation rates revealed that absence of lamin A is associated with high proliferation rates and absence of lamin C with slow growth rate, hence implicating absence of A-type lamin expression in cancer progression.48 A proteomic profile between normal human oral keratinocytes and oral squamous cell carcinomas derived cell lines found that twenty-two proteins were differentially expressed including proteins like annexin A1, heat shock protein 27 and lamin A/C.49 These investigations explore a possible avenue for A-type lamins as a signature molecule for oral cancer diagnosis.

Role of lamins in ovarian cancer

Recently, in a proteomic exploration to identify potential biomarkers for ovarian cancer (OC) in women with polycystic ovary syndrome (PCOS), tissue samples from women with and without OC were compared. The authors found that six biomarkers calreticulin, fibrinogenγ, superoxide dismutase, vimentin, malate dehydrogenase, and lamin B2 were overexpressed both in women with OC and in women with PCOS. These biomarkers could help identify the possible risk of ovarian cancer in women with PCOS.50 Further studies would be necessary to evaluate the true potential of these biomarkers.

Role of lamins in progeria disorder

Progeria or premature aging is a severe systemic disorder caused by mutations that lead to altered lamin A processing that leads to formation of a truncated protein progerin. Progerin also accumulates in different tissues of normal individuals as they age, suggesting it has a role in normal aging.51 Aging also leads to genomic instability, which is one of the leading risk factor for cancers, raising speculations about correlation between progerin and cancer. Mouse models in which cells accumulate prelamin A could help establish the relationship between prelamin A accumulation and invasive properties of cancer. Silencing of gene ZMPSTE24 in breast, oral, and lung cancer model causes progerin accumulation and changes in proteoglycan synthesis pathway leading to increased production of over-sulfated forms of chondroitin sulfate and heparan sulfate. These changes in the ECM components could lead to reduced invasive potential and establish progerin as a safeguard against cancer. Experiments performed in mosaic mouse models comprising of both prelamin A and normal mature lamin A expressing cells indicate that prelamin A does not affect tumor initiation, but suggests that it prevents cancer invasion.51 Another study investigating the role of progerin in human prostate, breast and colon cancer cell lines detected higher than normal expression of progerin in cancer cells. Ectopic progerin expression does not cause cellular senescence in cancer cells, and this could be attributed to defective DNA damage repair associated with progeria. Based on these results the authors hypothesize that progerin could promote tumor formation by increasing either DNA damage or genomic instability.52 However, no thorough clinical investigation to corroborate progerin’s role in cancer has been made, possibly due to quite a short lifespan of progeria patients.

Lamins—prognostic or diagnostic biomarker?

Cell motality, cell migration, and invasion are one of the critical fac-
tors during the progression of metastasis. Various studies have already indicated that undeniably lamin A/C is involved in cell proliferation, migration and invasion of various cancer cells. Enlargement and distortion of nuclear shape are characteristic features of a malignant cell also. As lamins play a vital role in providing structural and mechanical strength to the nucleus, their role in cancer has been under considerable scrutiny. Lamins often show aberrant expression and localization in cancer cells as shown in Table 1. Aberrant localization of lamin A/C to cytoplasm has been observed in various cancers like lung, colorectal and gastric cancers.21,26,39

Lamins are also shown to regulate oxidative stress in the cancer cells.60 While the low level ROS induces cell proliferation, increased ROS often results in DNA damage. ROS also acts as a basic signaling molecule in both the normal and cancer cells. Radiation or chemotherapeutic agents induced bystander effect is also mediated mostly by ROS.57-60 However, the role of lamin in cancer cell and bystander cells has to be elucidated in detail. The regulation of DNA damage and repair proteins, especially DNA double strand break repair proteins like ATM, ATR, H2AX,61 BRCA1, FANCD2 62-64 has to be tightly regulated to avoid the genomic instability and carcinogenesis. The dysregulation of A-type lamins impacts transcription, DNA replication and repair, and epigenetic modification of chromatin, hence inducing genomic instability that can contribute to cancer progression.65 Thus, it will be quite interesting to study the nuclear and cytoplasmic role of lamins in cancer progression and its recurrence. Role of lamins in both promotion and inhibition of apoptosis suggests a strong correlation between expression of lamins and malignancy of tumor cells.66

The current ambiguity in assigning lamins as a cancer biomarker is due to its variable expression between cancer subtypes.67 It is well known that Lamin B is universally expressed in many cell types, even cancer cells, making them a poor diagnostic marker for most studies except in the case of HCC where its overexpression is observed in both early and late stages of cancer. Similarly, lamin A/C might not serve as a useful diagnostic biomarker due to the variability between cancer subtypes. Larger statistical studies are necessary before clinical diagnosis utilizes aberrant expression or localization of lamins as a diagnostic biomarker for cancer.

Differentiation of tumor cells correlates with cancer prognosis, with higher differentiation correlating with better prognosis and low differentiation leading to poor prognosis.67 Lamin B potential to become a prognosis marker has been well studied in case of prostate and pancreatic cancer where it is associated with the more malignant form of cancer. Expression of lamin A/C is often used to demarcate differentiated cancer cells. Lamin A/C expression is also shown to alter expression of E-cadherin, which leads to reduced cell adhesion. Increase in cancer cell motility leads to metastasis and hence significantly worsens the prognosis.65 Therefore, based on the subtype of cancer involved lamin A/C has the potential to be a cancer biomarker, but detailed mechanistic investigations for the role of lamins in cancers are still wanting. This also indicates that lamins can be also used as prognostic marker in combination with other cancer markers. The role of Progerin in development of cancer is also not well elucidated and this could be another important area where we have to emphasize more. It will be also interesting to study the role of other nuclear lamin related protein like emerin and LAP2 alpha (Lamina-associated polypeptide 2 ) which also overexpressed in various cancer cells. The cross talk between these proteins and lamins are not so well studied.

### Table 1. Role of different types of lamins in various types of cancers.

| Type of cancer                | Type of lamins involved | Phenotype of lamin | Changes in nuclear shape/size |
|------------------------------|-------------------------|--------------------|-------------------------------|
| Hepatocellular carcinoma     | Lamin B                 | Increased expression of Lamin B | Enlargement of nucleus |
| Prostate cancer              | Lamin                   | Increased expression of lamin B | Enlargement of nucleus |
| BCC                          | Lamin A/C               | Low expression of Lamin A/C | Enlargement of nucleus |
| Colon cancer (Later stages)  | Lamin A/C               | Low expression of Lamin A/C | Enlargement of nucleus |
| Gastrointestinal Neoplasms   | Lamin A/C               | Aberrant or decreased Lamin A/C expression | Enlargement of nucleus |
| Gastric carcinoma            | Lamin A/C               | Decreased Lamin A/C mRNA and protein expression | Enlargement of nucleus |
| Breast cancer                | Lamin C                 | Decreased Lamin A/C expression | Enlargement of nucleus |
| Neuroblastoma                | Lamin A/C               | Decreased Lamin A/C expression | Enlargement of nucleus |

### Conclusions

In conclusion, lamin is over expressed in most of the cancers and has the ability to maintain the cancer cells homeostasis. Especially, lamin maintains the cell differentiation, proliferation and motility in tumors, which is essential for aggressive tumors. Conversely, contradicting results exist regarding role of lamins in cancer. This ambiguity could be answered by considering the numerous diverse functions that lamins perform in the cell and to relate its expression pattern in context to its role in cancers that arise from different cell types. As highlighted in the present review, lamin can be a potential diagnostic biomarker compared to prognostic marker. However, ‘bench to bedside’ approach to correlate large number of clinical samples and lamin expression analysis in these clinical samples can provide a better insight for cancer diagnostics.

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