REVIEW

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What is the Role of SNORA42 in Carcinogenesis? A Systematic Review

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Abstract

Objective: Perform a systematic literature review on SNORA42 in carcinogenesis in order to elucidate its importance, its potential use as a biomarker and as a therapeutic target. **Methods:** Using PubMed, SciELO and Science Direct databases as search means, articles that are in line with the scope of the study, written in English, that were published between 2012 and 2022, were selected using the following keywords: "small nucleolar RNA 42", "snoRNA 42" and "SNORA42", as well as searches for the synonyms of this snoRNA (SNORA80E, box H/ACA 42 and ACA42). **Result:** From a total of 131 studies, seven were selected, in which it was possible to identify that SNORA42 interferes in several biological processes, such as proliferation, migration, invasion, metastasis, apoptosis, and signaling pathways. Among the signaling pathways, the p53 and NF-KappaB pathways stand out. Moreover, it is a potential biomarker for diagnosis, prognosis, and treatment of cancer. **Conclusion:** The summary of the main information about SNORA42 in the process of carcinogenesis and cancer progression shows that the use of this snoRNA is ideal for future applications in the field of oncology, in which it can be used as a biomarker and therapeutic target. Thus, it is of fundamental importance to carry out new studies to consolidate the applicability of this molecule.

Keywords: Malignant Neoplasms- snoRNA- Biomarker

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Introduction

Small nucleolar RNAs (snoRNAs) are non-coding RNAs (ncRNAs), usually located in intronic regions. SnoRNAs are classified based on their specific sequence and secondary structural characteristics (Calvo e Köhn, 2021). In addition, snoRNAs can be associated with some long non-coding RNAs (LncRNAs), such as SNHGs-small nucleolar host gene (Zhu et al., 2019).

Early studies on snoRNAs reported that these molecules are present in a variety of eukaryotic organisms, being one of the most abundant groups of ncRNAs (Kiss, 2002). These ncRNAs accumulate mainly in the nucleoli, are 60-300 nucleotides (nts) in size, and are divided into three main families: C/D box (SNORDs), H/ACA box (SNORAs), and SCARNAs. The scaRNAs are localized molecules in a specialized subnuclear organelle known as the Cajal body (Enwerem et al., 2014; Cao et al., 2018).

In Figure 1 it can be seen that SNORDs are characterized by conserved C (RUGAUGA) and D (CUGA) sequences, and also by divergent copies of these boxes, C' and D ′. SNORAs are characterized by two single-stranded clip-like structures containing the H-box (ANANNA) and followed by a short tail containing the ACA (Wajahat et al., 2021). The scaRNAs, however, can be found as C/D box, H/ACA box or as a hybrid molecule of these two classes (Wajahat et al., 2021).

The snoRNAs have several functions, commonly classified according to their types: (i) SNORDs, act on the methylation of the 2'- O - ribose RNAs, (ii) SNORAs, direct the pseudouridylation of nts (Liang et al., 2019) and (iii) SCARNAs, direct the methylation of 2'-O and the pseudouridylation of the small nuclear RNAs (snRNAs) U1, U2, U4 and U5 (Darzacq et al., 2002).

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McMahon et al., (2019) reported that snoRNAs exert crucial functions in ribosome biogenesis, especially through complementarity of C/D and H/ACA snoRNAs to target rRNAs.

Like the other snoRNAs, SCARNAs have broad functionality, highlighting critical roles in spliceosome formation and ribosome maturation through modification at snRNAs and rRNAs (Marz et al., 2011; Massenet et al., 2017). The functions of these biomolecules are not yet fully understood, although studies suggest that the expression and activity of snoRNAs are altered in several human diseases, including cancer (Bellodi et al., 2013).

Furthermore, these ncRNAs also have non-canonical functions. Studies report that there are RNAs derived from snoRNAs (known as sdRNAs) that can act in functions similar to that of microRNAs and piRNAs (Chow and Chen, 2018; Abel and Rederstorff, 2019). Thus, sdRNAs would be able to regulate gene expression, associate with argon proteins, and influence translation in various pathologies, such as cancer (Falaleeva and Stamm, 2013; Okugawa et al., 2017). Among the snoRNAs that have a similar role to microRNAs, we can mention: ACA45, which generates microRNAs with the capacity to inhibit CDC2L6 activity; and SNORD75, which has the role of a piRNA, henceforth called pi-sno-75 (Ender et al., 2008; He et al., 2015; Barbosa et al., 2022)

Alterations in the expression profile of snoRNAs in human cancers have raised hypotheses about the participation of these snRNAs in cancer genesis and progression, such as SNORA42 (Okugawa et al., 2017). The literature has shown that this snoRNA is overexpressed in cancers and also participates in signaling pathways, such as the p53 pathway. With this, the present study aimed to conduct a systematic review involving SNORA42 (ACA42) expression data in cancer, discussing its function, importance, and potential as a therapeutic target.

Materials and Methods

Study Design

The present study is a systematic literature review registered in the International Prospective Register of Systematic Reviews (PROSPERO- https://www.crd.york.ac.uk/PROSPERO/) under number CRD42022363045. The study followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyzes (PRISMA - https://www.prisma-statement.org//) (Page et al., 2021).

Purpose of the Study

The guiding question of the study was: What is the participation of SNORA42 in carcinogenesis? To answer this question, we used the anagram PICOS, which considers: (i) Population (patients diagnosed with cancer); (ii) Intervention (overexpression of SNORA42 interfering with cancer progression); (iii) Comparison (not applicable); (iv) Outcome (Identify how SNORA42 influences worse prognostic factors and signaling pathways, targeting it as a potential biomarker and therapeutic target); (v) Study design (experimental studies).

Eligibility Criteria

Experimental studies published from 2012 to 2022 that addressed SNORA42 interference in cancer, and only articles in English, were considered eligible to be included in this systematic review. For this review, abstracts, reports, reviews, monographs, dissertations, observational articles, articles in another language, duplicate studies, incomplete studies, and non-accessible studies were excluded.

Data Sources and Strategies

The searches were performed in the following electronic databases: U. S. National Library of Medicine (PubMed), Scientific Electronic Library Online (SciELO) and Science Direct. In all databases we used the following descriptors: “small RNA nucleolar 42”, “snoRNA 42” and “SNORA42”. We also searched for synonyms of this snoRNA (SNORA80E, box H/ACA 42 and ACA42). The studies that contained the descriptors in the title, abstract and keywords were selected.

Study Selection and Strategies

For data selection, duplicates and studies that did not meet the exclusion criteria were removed. After the strategies were organized, the material was evaluated by two researchers individually and the results were compared. In case of divergent results, a third researcher was consulted. Data from each article were tabulated using Microsoft Excel 2019 software. The gray literature was also searched by accessing Google Scholar to find additional publications not detected in the selected electronic databases. For each study, the following information was considered: title, year, journal, main author, keyword, database, clinical and histopathological characteristics.

Quality Assessment

The quality of the methods used in the included studies was independently assessed by the researchers using the criteria of the Joanna Institute Critical Appraisal Tools (JBI). As represented in Table 01, for each criterion we considered the following classifications: “yes”, “no”, “unclear” and “not applicable”. The risk of bias classification was done according to the scores, being: from 1 to 3 “yes” (high bias risk); from 4 to 6 “yes” (moderate bias risk); and from 7 to 8 “yes” (low bias risk) (Mecenas et al., 2020).

Results

Survey and analysis of publications

There were 131 studies, of which 60 were excluded after analysis of duplicates and 33 after screening of titles and abstracts. A new filtering was performed, where seven review articles were identified and 15 more were excluded because they did not answer the study question or presented other languages. Thus, a total of seven studies (Table 2) were kept. The literature screening process is shown in Figure 2

After that, these papers went through the quality check-list for quasi-experimental studies, which considers nine

Table 1. Quality Assessment of the Methods Used in the Included Studies, Using Joanna Institute Critical Appraisal Tools (JBI)

Reference	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Total (Yes)	Bias Level
Mannoor, K. et al., 2014	Yes	Yes	No	Yes	Yes	*NA	NA	Yes	Yes	6	Moderate
Mei, Y.P. et al., 2012	Yes	Yes	No	Yes	Yes	NA	Yes	Yes	Yes	7	Low
Okugawa, Y. et al., 2017	Yes	Yes	**U	Yes	Yes	NA	NA	Yes	Yes	6	Moderate
Yi, C. et al., 2018	Yes	Yes	U	Yes	Yes	NA	Yes	Yes	Yes	7	Low
Wang, G. et al., 2021	Yes	Yes	U	Yes	Yes	NA	Yes	Yes	Yes	7	Low
Shan, Y. et al., 2021	Yes	Yes	No	Yes	Yes	NA	Yes	Yes	Yes	7	Low
Li, Y. et al., 2019	Yes	Yes	U	Yes	Yes	NA	Yes	Yes	Yes	7	Low

*NA, Not applicable; **U, Unclear

criteria, namely: (Q1) temporal relationship of variables, (Q2) difference between participants, (Q3) difference in approach received by groups, (Q4) existence of a control group, (Q5) comparison between outcomes measured before and after therapeutic intervention, (Q6) complete follow-up of each group, (Q7) equal measurement of outcomes for each group, (Q8) reliability of results, and (Q9) statistical analysis (JBI, 2020). Of the 7 studies analyzed only 2 have moderate bias and the rest have a low risk. Therefore, all papers were suitable to be included in the review (Table 1).

According to the research, the seven studies listed show that SNORA42 is overexpressed in six types of cancer and is associated with poor prognostic factors and biological functions such as cell proliferation, migration, invasion, and apoptosis (Table 2).

As for the participation of SNORA42 in biological pathways, research has shown that this snoRNA has the potential to interfere in signaling pathways, especially activating NF-KappaB and p53 pathways in cancer. Fig. 03 summarizes the main findings of this snoRNA in signaling pathways.

Discussion

Biological processes associated with cancer progression

Cancer progression requires several biological processes to occur, such as cell proliferation, cell migration, absence of apoptosis, and colony formation, (Anoushirvani et al., 2023). Cell proliferation is a key process in the formation of colonies in cancer. Migration and invasion, in turn, are features that allow cancer cells

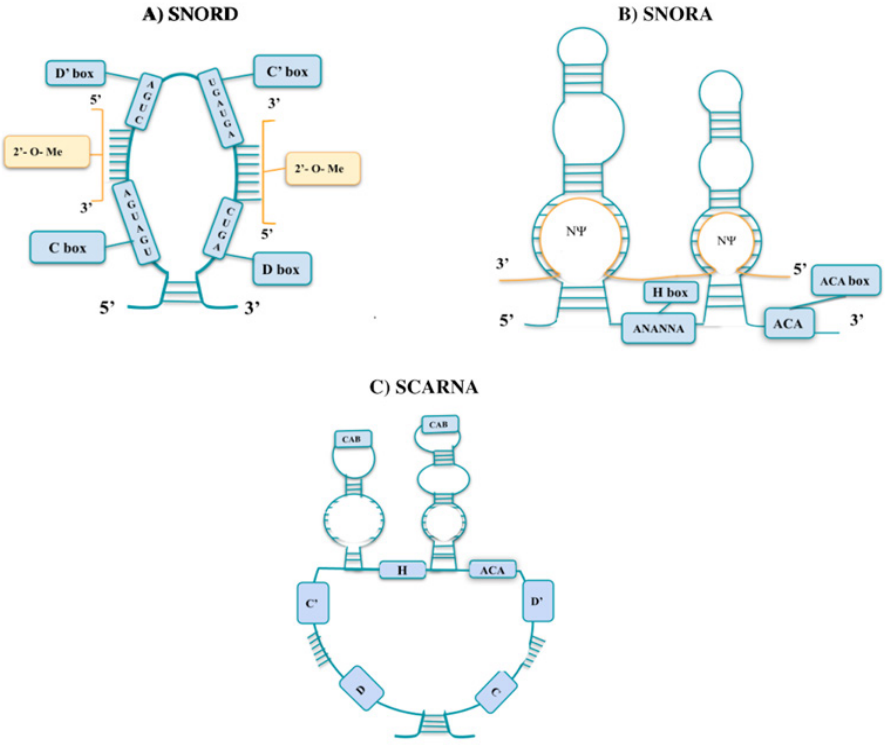

Figure 1. Families of snoRNAs - SNORD, SNORA and SCARNA: (A) represents the family of ORDs,characterized by conserved C (RUGAUGA) and D (CUGA) sequences, this class features 2'-O-methylated guided C/D box snoRNAs, consisting of the paired 5th base nucleotides upstream of the D or D' boxes. (B) Represents SNORAs, similar to a staple, this family contains an H-box (ANANNA) followed by a short tail containing the ACA, for H-box/ACA-box snoRNAs, the first unpaired nucleotides in each fold pseudouridylation pseudouridylation can occur at one or two distinct targets. (C) Represents SCARNAs, in which C/D and H/ACA hybridization is demonstrated, this class has a Cajal body-specific localization element (CAB box).

Table 2. Main Studies Evidencing the Participation of SNORA42 in Cancers

Reference	Expression type	Sample Type	Biological function and relationship with biological pathways	Clinical Meaning	Diagnostic, Prognostic and Treatment Indicators
Mannoor, K. et al., 2014	Overexpressed	Lung tumor tissue CPCNP cell lines.	Cell proliferation, migration, invasion, apoptosis, and colony formation.	Metastasis, worse survival.	Biomarker for diagnosis, prognosis and for treatment.
Mei, Y.P. et al., 2012	Overexpressed	Cell Lines Tumor and non-cancerous tissues	Cell proliferation, apoptosis, colony formation.	TNM, worse survival.	Biomarker for diagnosis, prognosis and treatment.
Okugawa, Y. et al., 2017	Overexpressed	Colorectal tissues	Cell proliferation, migration, invasion, apoptosis, colony formation.	Metastasis, TNM, worse survival.	Biomarker for diagnosis, prognosis and treatment.
Yi, C. et al., 2018	Overexpressed	CaP cells	Cell proliferation, migration, invasion and apoptosis.	Metastasis, TNM, worse survival.	Treatment
Wang, G. et al., 2021	Overexpressed	Tissue Human HCC cell lines. Human Liver Cell Lines	Cell proliferation, migration, invasion and apoptosis. Inhibition of the p53 pathway	TNM, worse survival.	Biomarker for prognosis and treatment.
Shan Y, et al., 2021	Overexpressed	All cell lines CCEE and immortalized human esophageal epithelial cells.	Cell proliferation, migration, invasion and apoptosis. NF-kB pathway down-regulated	Metastasis, TNM, worse survival.	Biomarker for prognosis and for treatment.
Li Y, et al., 2019	Overexpressed	Tumor and non-cancerous tissues. Human GC cell lines.	Cell proliferation, colony formation and apoptosis.	-	Prognostic biomarker.

to spread and invade other regions of the body, thereby triggering metastasis (Zanotelli et al., 2021). These processes are favored by a number of factors, including genetic mutations, alterations in non-coding RNAs, among others, that affect the cell's ability to adhere to other cells and the extracellular matrix, as well as factors in the tumor microenvironment, such as the presence of stromal cells and inflammatory molecules (Hanahan, 2022). In this work, it was possible to observe that the deregulation of SNORA42 is associated with biological processes that contribute to the development and progression of cancer, consequently triggering factors of worse prognosis.

The biological functions of SNORA42 with regard to migration, invasion, apoptosis and colony formation have been observed in both in vivo and in vitro experiments. In a study with lung cancer, it was observed that through assays for SNORA42 silencing there was inhibition of tumor growth in vitro and in vivo (Mei et al., 2012). In

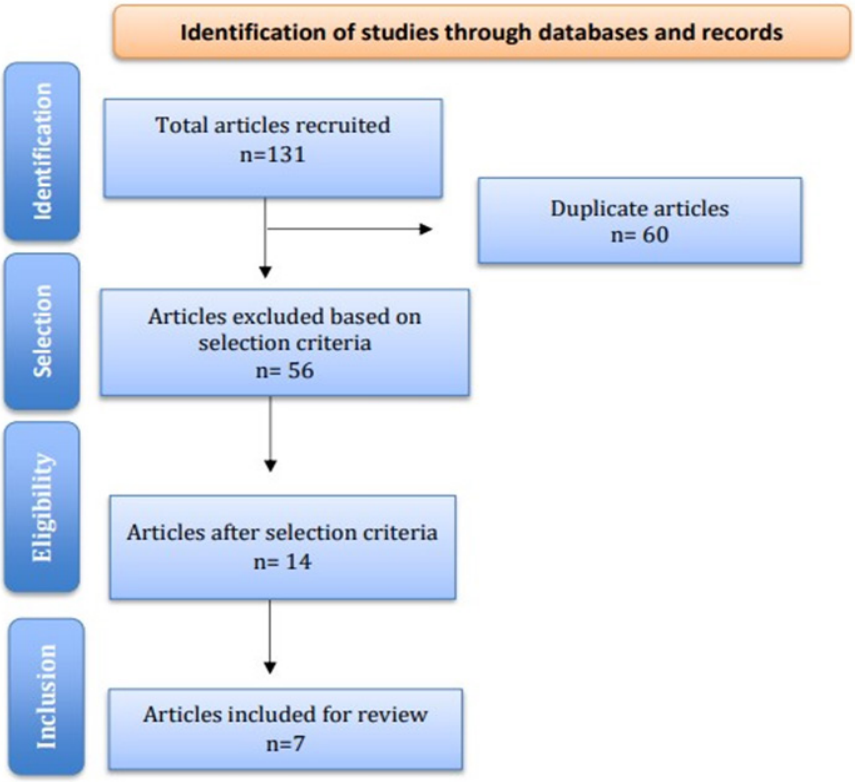

Figure 2. Flowchart of Article Selection

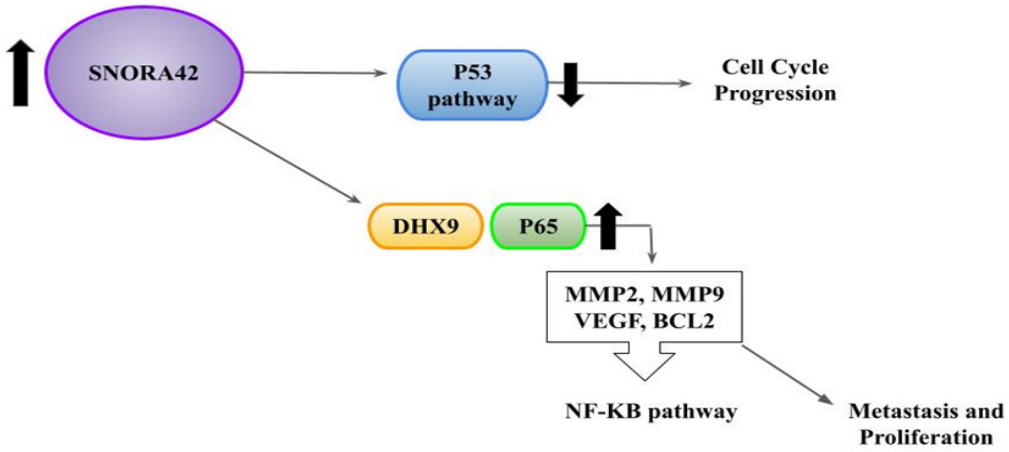

Figure 3.Association of SNORA42 with the p53 Pathway and NF-κB. The overexpression of SNORA42 interferes with signaling pathways such as p53, DHX9, and p65, where this interference promotes cell cycle progression and enables proliferation and metastasis.

another work, with hepatocellular cancer (HCC) cell lines, silencing of SNORA42 decreased proliferation, migration, and invasion, in vivo, in addition it was able to inhibit tumor growth and metastasis (Wang et al., 2021). Similar data to the above, were also observed in prostate cancer (Yi et al., 2018) and and colorectal cancer cell lines (Okugawa et al., 2017). The participation of this snoRNA in these processes, may be due to the co-expression of SNORA42 with genes involved that act in processes that trigger the carcinogenic process (Okugawa et al., 2017), as demonstrated by Li et al., (2019), whose inhibition of SRPK1, resulted in a decrease in SNORA42. Therefore, it is evident that SNORA42 may play an important role in the progression of several types of cancer, and that understanding the underlying molecular mechanisms may lead to new therapeutic approaches.

NF-kB pathway negatively regulated by SNORA42

SNORA42 can act in signaling pathways, in esophageal cancer (EC) it was possible to evidence that SNORA42 is able to interact and regulate DHX9 protein expression, promote its accumulation in the nucleus and attenuate its degradation via ubiquitination. This same work evidenced that overexpression of SNORA42 was able to increase the interaction of p65 with DHX9 and influence the expression of downstream genes of the NF-κB pathway (MMP2, MMP9, VEGFC and BCL2) (Shan et al., 2021). The p65 protein is involved in different processes during tumorigenesis, favoring growth, angiogenesis, and invasion of tumor cells (Ben-Neriah and Karin, 2011).

NF-κB signaling may assist in cancer progression by controlling the epithelial-mesenchymal transition and metastasis, NF-kB is often associated with the positive regulation of matrix metalloproteinases (MMPs), which act on the extracellular matrix, thus promoting tumor cell evasion. In addition, NF-κB may contribute to tumor progression by positively regulating VEGF (vascular endothelial growth factor) and its receptors (Hoesel and Schimid, 2013).

There are reports in the literature of anti-tumor therapies that target the NF-κB pathway. In this context, several anti-inflammatory drugs, such as aspirin, sodium salicylate, and dexamethasone, are used as therapeutics aiming to suppress NF-κB. However, this signaling pathway plays important functions in the immune response and prolonged use of NF-κB inhibitors can result in immunodeficiency (Yu et al., 2020). Furthermore, the association of NF-κB inhibitors and conventional therapies is necessary, as blocking NF-κB alone may not be sufficient for tumor regression (Yu et al., 2020). Thus, clinical trials supporting the use of SNORA42 inhibitors are needed, especially evaluating their effect with and without simultaneous action of NF-kB inhibitors.

In the p53 pathway, Wang et al., (2021), demonstrated that knockdown of SNORA42 in HCC resulted in decreased levels of p53 and p21 and increased levels of Cyclin E and Cyclin D. Opposite results were observed in experiments presenting this overexpressed snoRNA. In the cited study, SNORA42 promoted HCC progression by inhibition of the p53 signaling pathway. Silencing of p53 allows tumor cells to survive due to the impact of inducing apoptosis and DNA repair (Hernández and El-Deiry, 2021). However, the regulation of p53 by SNORA42 has not yet been elucidated.

As illustrated in Fig. 03, overexpression of SNORA42 induces inhibition of the p53 pathway, impacting cell cycle progression. Furthermore, increased expression of SNORA mediates the interaction between DHX9 and p65, positively regulating these proteins, which influence the expression of NF-kB pathway genes, such as MMP2, MMP9, VEGF, and BCL2. Based on the cited information, we evidenced that SNORA42 is an oncogenic snoRNA and its deregulation is involved with worse prognostic factors in several tumor types.

SNORA42 as a Potential Biomarker

A biomolecule is considered a biomarker when its presence, absence, or quantitative or qualitative changes in a biological tissue, fluid, or cell are associated with a specific pathological process, such as a disease. Biomarkers can be used to diagnose the presence or

progression of disease, monitor treatment efficacy and disease progression (Zou et al., 2019). The data presented in the articles demonstrate that SNORA42 is a potential biomarker.

Mannoor et al., (2014) demonstrated that overexpression of SNORA42 in non-small cell lung tumor samples, was related to decreased patient survival. In colorectal cancer similar data was found (Okugawa et al., 2017), moreover in this same work it was possible to observe that SNORA42 is a potential predictive biomarker for recurrence and unfavorable prognosis in colorectal cancer.

These data support a potential applicability of this snoRNA as a prognostic, diagnostic and therapeutic target biomarker in the mentioned tumors. Importantly, snoRNAs can be released from tumor cells via exosomes or after cell death in circulating fluids (Pardini et al., 2019). This makes SNORA42 detectable by non-invasive or minimally invasive techniques, such as obtaining sputum or plasma. Furthermore, SNORA42 appears to remain stable in these samples, which favors its use as a tumor biomarker (Mourksi et al., 2020). However, the correct characterization of snoRNA signatures at different tumor stages is crucial to understand the behavior of these molecules throughout disease progression (Mannoor et al., 2014).

Despite the evidence for the participation of SNORA42 in biological processes and its potential applicability as a diagnostic/prognostic and therapeutic target biomarker, there are gaps that need to be filled. The mechanisms used by this snoRNA, to influence the biological processes are poorly understood. Therefore, a better understanding of the epigenetic processes used by SNORA42 will be able to lead to advances in oncology.

SnoRNAs can be used as potential biomarkers for therapy, studies on ncRNAs show that these biomolecules have significant importance for the treatment of cancers, as well as for other pathologies several studies have been developed for the clinical application of RNA-based therapies, employing mainly antisense oligonucleotides (ASO) and small interfering RNAs (siRNAs), and several have obtained Food and Drug Administration (FDA) approval (Winkle et al., 2021).

Research reports that SNORA42-siRNA inhibited lung tumors in mice, thus showing its significant therapeutic potential, especially in inoperable cases. Moreover, the inhibition of SNORA42 can overcome the problem of drug resistance (Shan et al., 2021). In a work performed with another type of snoRNA, Cui et al., (2017) demonstrated that ASO-mediated inhibition of SNORA23 expression was able to reduce tumor growth, dissemination, and liver metastasis in pancreatic ductal adenocarcinoma xenografts. This demonstrates that snoRNAs may serve as potential targets for therapeutic drugs in oncology.

The understanding of the role of snoRNAs in cancer is still limited, mainly due to the scarcity of studies in the field. However, the few published studies are consistent and indicate an important role of this class of ncRNAs in cancer. These studies have demonstrated, by in vitro and in vivo assays, that the expression of some snoRNAs, such as SNORA42, has an oncogenic effect. Thus, considering the importance of snoRNAs as a prognostic factor and therapeutic potential, studies that aim to elucidate the mechanisms and pathways associated with these RNAs are fundamental and may enrich the knowledge about the genetic basis of cancer.

Author Contribution Statement

ESB, AGMM, AFM: Paper design; methodology; data collection; manuscript writing. MGOPS, MAS, CRTS, MAS, ASK, JMTB, AALTJr: Critical review and approval of the manuscript. JDP: Critical revision, editing, and approval of the manuscript; supervision of the work

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Study Registration

International Prospective Register of Systematic Reviews under number CRD42022363045.

Conflict of Interest

The authors declare no conflicts of interest.

References

Abel Y, Rederstorff M (2019) SnoRNAs and the emerging class of sdRNAs: Multifaceted players in oncogenesis. *Biochimie*, **164**, 17-21.

Anoushirvani A, Jafarian Yazdi A, Amirabadi S, et al (2023). Role of non-coding RNAs in neuroblastoma. *Cancer Gene Ther*, **2023**, 1-19.

Barbosa ES, Sousa LR, Matos AGM, et al (2022) Identificação das funções canônicas e não-canônicas de snornas associados a cânceres: Uma breve descrição da literatura. Agenda Global de Pesquisa em Ciências Biológicas. Atena, Ponta Grossa - PR, pp 96–107.

Bellodi C, McMahon M, Contreras A (2013). H/ACA small RNA dysfunctions in disease reveal key roles for noncoding RNA modifications in hematopoietic stem cell differentiation. *Cell Rep*, **3**, 1493-2.

Ben-Neriah Y, Karin M (2011). Inflammation meets cancer, with NF-κB as the matchmaker. *Nat Immunol*, **12**, 715-23.

Calvo SJ, Köhn M (2021). Small but Mighty-The Emerging Role of snoRNAs in Hematological Malignancies. *Noncoding RNA*, **7**, 68.

Cao T, Rajasingh S, Samanta S, et al (2018). Biology and clinical relevance of noncoding sno/scaRNAs. *Trends Cardiovasc Med*, **28**, 81.

Chow RD, Chen S (2018) Sno-derived RNAs are prevalent molecular markers of cancer immunity. *Oncogene*, **37**, 6442-62.

Cui L, Nakano K, Obchoei S, et al (2017). Small Nucleolar Noncoding RNA SNORA23, Up-Regulated in Human Pancreatic Ductal Adenocarcinoma, Regulates Expression of Spectrin Repeat-Containing Nuclear Envelope 2 to Promote Growth and Metastasis of Xenograft Tumors in Mice. *Gastroenterology*, **153**, 292-6.

Darzacq X, Jády BE, Verheggen C et al (2002). Cajal body-specific small nuclear RNAs: a novel class of

2'-O-methylation and pseudouridylation guide RNAs. *EMBO J*, **21**, 2746-56.
Ender C, Krek A, Friedländer MR, et al (2008) A human snoRNA with microRNA-like functions. *Mol Cell*, **32**, 519-28.
Enwerem II, Velma V, Broome HJ, et al (2014). Coilin association with Box C/D scaRNA suggests a direct role for the Cajal body marker protein in scaRNP biogenesis. *Biol Open*, **3**, 240-9.
Falaleeva M, Stamm, S. (2013) Processing of snoRNAs as a new source of regulatory non-coding RNAs: snoRNA fragments form a new class of functional RNAs. BioEssays: news and reviews in molecular, cellular and developmental biology. **35**, pp 46–54.
Hanahan D (2022). Hallmarks of Cancer: New Dimensions. *Cancer Discovery*, **12**, 31–46.
He X, Chen X, Zhang X, et al (2015) An Lnc RNA (GAS5)/ SnoRNA-derived piRNA induces activation of TRAIL gene by site-specifically recruiting MLL/COMPASS-like complexes. *Nucleic Acids Res*, **43**, 3712–25.
Hernández BLJ, El-Deiry WS (2021). Tumor suppressor p53: Biology, signaling pathways, and therapeutic targeting. *Biochim Biophys Acta Rev Cancer*, **1876**, 188556.
Hoesel B, Schmid JA (2013). The complexity of NF-κB signaling in inflammation and cancer. *Mol Cancer*, **2**, 12-86.
International Prospective Register of Systematic Reviews. (2018) How to register [Internet]. International Prospective Register of Systematic Reviews Disponível em: https://www.crd.york.ac.uk/prospero/.
Joanna Briggs Institute. Critical appraisal tools, (2020). Disponível em: https://jbi.global/critical-appraisal-tools
Kiss T (2002). Small nucleolar RNAs: an abundant group of noncoding RNAs with diverse cellular functions. *Cell*, **109**, 145-8.
Li Y, Yu S, Wang X, et al (2019). SRPK1 facilitates tumor cell growth via modulating the small nucleolar RNA expression in gastric cancer. *J Cell Physiol*, **234**, 13582-91.
Liang J, Wen J, Huang Z (2019). Small Nucleolar RNAs: Insight Into Their Function in Cancer. *Front Oncol*, **9**, 587.
Mannoor K, Shen J, Liao J, et al (2014) Small nucleolar RNA signatures of lung tumor-initiating cells. *Mol Cancer*, **6**, 104.
Marz M, Gruber AR, Höner ZSC, et al (2011). Animal snoRNAs and scaRNAs with exceptional structures. *RNA Biol*, **8**, 938-6.
Massenet S, Bertrand E, Verheggen C (2017). Assembly and trafficking of box C/D and H/ACA snoRNPs. *RNA Biol*, **14**, 680-2.
McMahon M, Contreras A, Holm M, et al (2019). A single H/ACA small nucleolar RNA mediates tumor suppression downstream of oncogenic RAS. *Elife*, **8**, 48847.
Mecenas P, Bastos RTDRM, Vallinoto ACR, et al (2020). Effects of temperature and humidity on the spread of COVID-19: A systematic review. *PLoS One*, **15**, e0238339.
Mei YP, Liao JP, Shen J, et al (2012). Small nucleolar RNA 42 acts as an oncogene in lung tumorigenesis. *Oncogene*, **31**, 2794-804.
Mourksi NEH, Morin C, Fenouil T, Diaz JJ, Marcel V (2020). snoRNAs Offer Novel Insight and Promising Perspectives for Lung Cancer Understanding and Management. *Cells*, **9**, 541.
Okugawa Y, Toiyama Y, Toden S, et al (2017). Clinical significance of SNORA42 as an oncogene and a prognostic biomarker in colorectal cancer. *Gut*, **66**, 107-17.
Page MJ, McKenzie JE, Bossuyt PM, et al (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ*, **372**, n71.
Pardini B, Sabo A, Birolo G, et al (2019). Noncoding RNAs in extracellular fluids as cancer biomarkers: the new frontier of liquid biopsies. *Cancers*, **11**, 1170.
Shan Y, Wei S, Xiang X, et al (2021). SNORA42 promotes oesophageal squamous cell carcinoma development through triggering the DHX9/p65 axis. *Genomics*, **113**, 3015-29.
Wajahat M, Bracken CP, Orang A (2021). Emerging Functions for snoRNAs and snoRNA-Derived Fragments. *Int J Mol Sci*, **22**, 10193.
Wang GG, Li J, Yao Y, et al (2021). Small nucleolar RNA 42 promotes the growth of hepatocellular carcinoma through the p53 signaling pathway. *Cell Death Discov*, **7**, 347.
Winkle M, El-Daly SM, Fabbri M, Calin GA (2021). Noncoding RNA therapeutics - challenges and potential solutions. *Nat Rev Drug Discov*, **20**, 629-51.
Yi C, Wan X, Zhang Y, et al (2018). SNORA42 enhances prostate cancer cell viability, migration and EMT and is correlated with prostate cancer poor prognosis. *Int J Biochem Cell Biol*, **102**, 138-50.
Yu H, Lin L, Zhang Z, Zhang H, Hu H (2020). Targeting NF-κB pathway for the therapy of diseases: mechanism and clinical study. *Signal Transduct Target Ther*, **21**, 209.
Zanotelli M, Zhang J, Reinhart-King C (2021). Mechanoresponsive metabolism in cancer cell migration and metastasis. *Cell Metabolism*, **33**, 1307–21.
Zou, J, Wang E (2019). Cancer Biomarker Discovery for Precision Medicine New Progress. *Curr Med Chem*, **26**, 7655–71.
Zhu Q, Yang H, Cheng P, Han Q (2019). Bioinformatic analysis of the prognostic value of the lncRNAs encoding snoRNAs in hepatocellular carcinoma. *Bio Factors (Oxford, England)*, **45**, 244–2.