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Research on spinocerebellar ataxia type 2 in Cuba: a bibliometric analysis

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ABSTRACT

Introduction: Spinocerebellar Ataxia Type 2 is a hereditary neurodegenerative disorder. Over the past three decades, Cuban researchers have significantly advanced in the understanding of it. Their contributions span epidemiological surveillance, genetic and molecular research, biomarker discovery, clinical characterization, and therapeutic strategies. **Objective:** To provide a comprehensive bibliometric analysis of Spinocerebellar Ataxia Type 2 research in Cuba from 1996 to 2024. **Methods:** The study utilized data from 71 articles and reviews on Spinocerebellar Ataxia Type 2, accessed through the Web of Science database. VOS viewer software was employed to analyze keyword co-occurrence, co-author, and institutional co-llaboration networks. Co-word analysis identified thematic shifts, while co-authorship and institutional networks mapped collaboration patterns across national and international part-ners. **Results:** Results show an evolution in Cuban Spinocerebellar Ataxia Type 2 research from initial genetic studies focused on CAG repeat expansions in the ATXN2 gene to recent patient-centered clinical research, emphasizing diagnosis, biomarkers, and disease progression. Key institutions such as the Center for Research and Rehabilitation of Hereditary Ataxias, Cuban Academy of Sciences, and Cuban Center for Neurosciences emerged as primary research hubs, with longstanding collaborations involving German institutions. Newer partnerships with Latin American institutions, particularly the National Autonomous University of Mexico, reflect a regional focus on population-specific studies. **Conclusions:** The thematic progression in Spinocerebellar Ataxia Type 2 research reflects a shift toward translational and patient-focused approaches. Cuban-led Spinocerebellar Ataxia Type 2 research exemplifies successful international and regional collaboration, providing a model for tackling complex, population-specific health issues. Continued efforts in biomarker discovery, therapeutic development, and clinical applications are essential for advancing patient care and research impact in Spinocerebellar Ataxia Type 2. This bibliometric study offers strategic insights for guiding future research directions in Spinocerebellar Ataxia Type 2.

Keywords: Bibliometric analysis; Cuban research collaboration; Genetic and clinical research; Inter-national partnerships; Spinocerebellar Ataxia Type 2

Investigación sobre la ataxia espinocerebelosa tipo 2 en Cuba: un análisis bibliométrico

RESUMEN

Introducción: La Ataxia Espinocerebelosa Tipo 2 es un desorden neurodegenerativo hereditario. Durante las 3 décadas pasadas los investigadores cubanos han avanzado significativamente en la comprensión de este desorden. Sus contribuciones abarcan la vigilancia epidemiológica, investigación genética y molecular, descubrimiento de biomarcadores, caracterización clínica y estrategias terapéuticas. **Objetivo:** Presentar un análisis bibliométrico de la investigación sobre la Ataxia Espinocerebelosa Tipo 2 en Cuba entre 1996 y 2024. **Métodos:** Se analizaron 71 artículos y revisiones sobre Ataxia Espinocerebelosa Tipo 2 extraídos de la base de datos ***Web of Science***. Se utilizó el ***software*** VOSviewer para examinar la coocurrencia de palabras clave, las redes de coautoría y colaboración institucional. El análisis de copalabras permitió identificar cambios temáticos, mientras que las redes colaborativas revelaron los vínculos entre instituciones y autores, tanto nacionales como internacionales. **Resultados:** La investigación en Cuba sobre Ataxia Espinocerebelosa Tipo 2 ha transitado desde estudios genéticos centrados en las expansiones de repeticiones CAG en el gen *ATXN2* hacia investigaciones clínicas orientadas al diagnóstico, biomarcadores y progresión de la enfermedad. Instituciones como el Centro para la Investigación y Rehabilitación de las Ataxias Hereditarias, la Academia de Ciencias de Cuba y el Centro Cubano de Neurociencias han sido actores clave. Las colaboraciones sostenidas con universidades alemanas y nuevas alianzas con instituciones latinoamericanas, como la Universidad Nacional Autónoma de México, evidencian un enfoque integrador y regional. **Conclusiones:** La evolución temática refleja un giro hacia enfoques traslacionales y centrados en el paciente. La investigación cubana sobre la Ataxia Espinocerebelosa Tipo 2 destaca por su modelo colaborativo internacional y regional. Los esfuerzos en biomarcadores, terapias y aplicaciones clínicas serán fundamentales para mejorar el manejo de la enfermedad y guiar futuras investigaciones.

Palabras clave: análisis bibliométrico; colaboración científica cubana; investigación genética y clínica; alianzas internacionales; Ataxia Espinocerebelosa tipo 2

INTRODUCTION

Spinocerebellar Ataxia Type 2 (SCA2) is a hereditary neurodegenerative disorder characterized by progressive ataxia, intentional tremors, dysarthria, oculomotor dysfunction, autonomic disturbances, and cognitive decline. [1,2,3,4] The disease is caused by an abnormal expansion of CAG trinucleotide repeats in th *ATXN2* gene, leading to toxic protein aggregation and progressive neurodegeneration, particularly in cerebellar and brainstem structures. [1,5] SCA2 is the second most common autosomal dominant ataxia worldwide and exhibits the highest known prevalence in specific regions of eastern Cuba, where it presents a considerable public health and socio-economic burden. [4]

Over the past three decades, Cuban researchers have significantly advanced the understanding of SCA2. Their contributions span epidemiological surveillance, genetic and molecular research, biomarker discovery, clinical characterization, and therapeutic strategies. [5,6,7] These efforts have not only informed local healthcare policies but have also contributed to the global body of knowledge on polyglutamine (polyQ) neurodegenerative diseases. [8,9,10]

Early Cuban studies established the association between CAG repeat length and age of onset and severity of SCA2. [11] Further genetic research explored regulatory regions of ATXN2, such as CpG islands in exon 1, revealing new insights into gene expression and potential targets for molecular therapies. [11,12] Parallel advances in biomarker research have identified electrophysiological indicators capable of detecting neurodegeneration up to 15 years before clinical onset, categorized into preclinical, progression, and genetic damage markers. [13] Oxidative stress, extensively studied in SCA2, emerged as a key pathophysiological mechanism and a potential therapeutic target. [7,14] Alterations in sleep micros-

tructure —specifically sleep spindles and K-complexes— have also been linked to disease progression, suggesting polysomnography as a valuable monitoring tool. [15,16]

Clinically, SCA2 presents a complex phenotype, with cerebellar ataxia, slowed saccadic eye movements, tremors, cognitive impairment, and other sensory deficits. [13] Neuropathological investigations have shown extensive degeneration in the cerebellum, brainstem, and cranial nerve nuclei, including significant loss of Purkinje cells and deep cerebellar nuclei—pathological hallmarks that underpin the clinical manifestations of the disease. [5,17,18]

Therapeutically, Cuban studies have pursued both neuroprotective and symptomatic interventions. A phase I–II clinical trial of intranasal NeuroEPO demonstrated safety and moderate clinical benefits in SCA2 patients. [19] Neurorehabilitation programs have proven effective in improving motor symptoms, and antioxidant therapies have shown promise in reducing oxidative damage and slowing disease progression. [17,18,19,20,13]

Beyond clinical and molecular research, Cuban scientists—especially Velázquez-Pérez and Rodríguez-Labrada—have led impactful public health initiatives. These include presymptomatic testing (PST), genetic counseling, and prenatal diagnosis (PND), reaching over 1,000 individuals and providing reproductive options to families at risk. Such programs, which have demonstrated high acceptance rates, are vital in low-resource settings where access to preimplantation genetic diagnosis remains limited. [21,22] These initiatives have helped integrate the management of genetic disorders into Cuba's broader public health infrastructure. [23]

Despite this progress, no comprehensive bibliometric study has been conducted to systematize the scientific production on SCA2 in Cuba. Such an analysis is essential for mapping thematic trends, identifying key contributors and institutional networks, and uncovering research gaps. It would provide strategic insight for directing future research, guiding policy decisions, and optimizing resource allocation.

The objective of this study is to provide a comprehensive bibliometric analysis of SCA2 research in Cuba, highlighting thematic trends, key collaborative networks, and the evolution of research priorities from 1996 to 2024.

METHODS

This study's dataset comprises 71 research articles and review articles sourced from the Web of Science (WoS) Core Collection, covering the period from 1996 to November 1, 2024 published by Cuban scientists. The search criteria used included "Spinocerebellar Ataxia Type 2" in the title and restricted the document types to articles and reviews. Data collection was conducted through the WoS platform.

Mapping and Analysis Procedure

The methodological framework integrated co-word analysis and VOSviewer software, selected for their complementary strengths in uncovering thematic structures and visualizing complex bibliometric data. [24,25] Co-word analysis enabled the identification of recurrent research themes and focal points by examining the frequency and co-occurrence of keywords, thereby revealing core conceptual areas and their interrelationships. This method also facilitated the tracking of thematic evolution over time, offering critical insights into shifts in research priorities. Furthermore, it allowed the detection of thematic clusters, mapping distinct subfields and outlining the intellectual structure of the domain. By combining quantitative metrics with qualitative interpretations, co-word analysis provided a comprehensive understanding of research dynamics within the field.

VOSviewer, in turn, contributed robust visualization capabilities, constructing detailed and interpretable maps of bibliometric networks such as co-authorship, co-citation, and keyword co-occurrence. Its flexible and user-friendly design supported the customization and in-depth exploration of data, enhancing interpretability and analytical depth. The combined use of these tools offered several advantages: precise identification of prevailing trends, visualization of complex thematic relationships, and effective handling of large publication datasets. Importantly, the temporal dimension of this approach not only illuminated the historical development of research themes but also suggested potential future trajectories within the field.

Steps for Quantitative Analysis

Data Preprocessing: To ensure accuracy, the data was reviewed to remove duplicates and irrelevant entries. Keywords were standardized for consistency across the dataset. Building Bibliometric Maps: Keyword co-occurrence matrices were generated, and VOSviewer was used to construct and visualize the resulting bibliometric maps. This methodological approach provides a rigorous, in-depth analysis of thematic evolution, key research areas, and collaboration dynamics, offering a comprehensive understanding of the research field's development.

RESULTS

Evolution of Research Dynamics in Spinocerebellar Ataxia Type 2 in Cuba

Figure 1 illustrates the evolving trajectory of Spinocerebellar Ataxia Type 2 (SCA2) research in Cuba, highlighting a progressive shift from foundational genetic inquiries to clinically oriented investigations over the past 15 years. The initial pha-

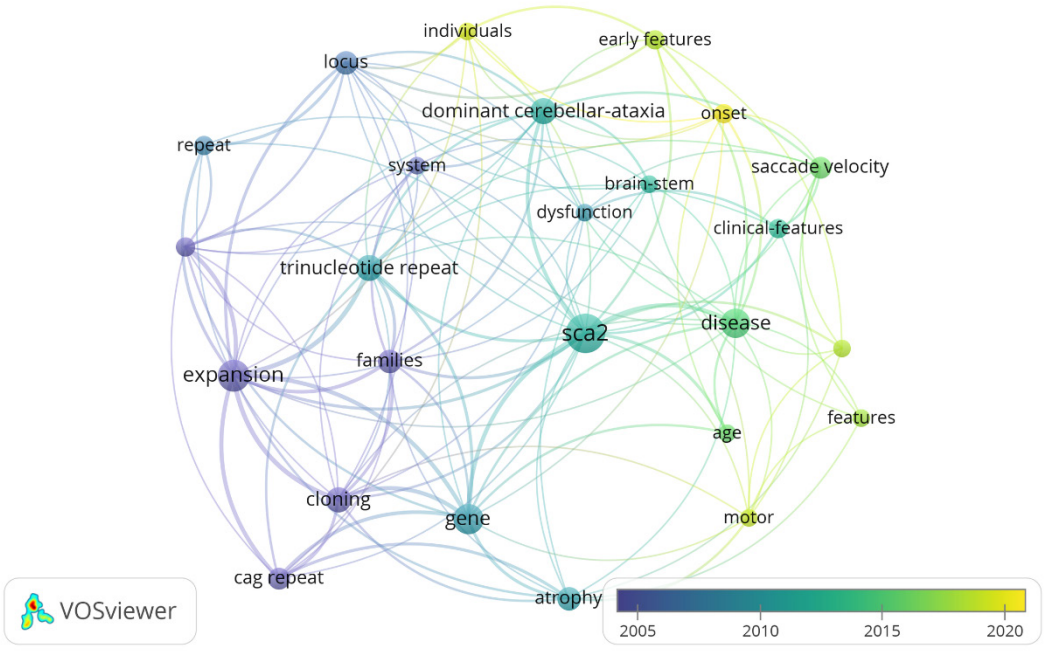

Fig 1. Evolution of Research Trends in Spinocerebellar Ataxia Type 2 (SCA2) from 2005 to 2020

se of research was primarily concerned with elucidating the genetic basis of SCA2, particularly the pathological expansion of CAG trinucleotide repeats within the *ATXN2* gene an essential determinant of disease onset and penetrance. This genetic focus laid the groundwork for subsequent studies examining the pathophysiological consequences of these mutations, notably their impact on neuroanatomical structures such as the brainstem and cerebellum. These investigations underscored progressive atrophy in these regions as key neuropathological hallmarks of the disease.

As the scientific agenda matured, Cuban researchers increasingly redirected their attention toward translational and patient-centered approaches. Recent studies have emphasized the development and validation of clinical biomarkers —including saccade velocity, motor performance indices, and age of symptom onset— as tools for early diagnosis, disease stratification, and longitudinal monitoring. This evolution reflects not only a broadening of methodological frameworks but also a commitment to integrating molecular, neurodegenerative, and clinical domains in a coherent research paradigm. Overall, figure 1 captures this multidimensional transformation, offering a visual synthesis of how SCA2 research in Cuba has transitioned from molecular genetics to applied clinical neuroscience, thereby enhancing both scientific understanding and healthcare outcomes for affected populations.

Stage 2005-2010 (Genetics and Molecular Mechanisms)-Dark Blue to Teal Nodes

During the initial phase of Cuban research on Spinocerebellar Ataxia Type 2 (SCA2), spanning from 2005 to 2010, the scientific focus was predominantly centered on genetic discovery and the elucidation of underlying molecular mechanisms. This period was marked by intensive investigation into the role of CAG trinucleotide repeat expansions in the ATXN2 gene, which emerged as the primary genetic determinant of disease onset. Key research efforts were directed toward identifying the specific gene locus responsible for SCA2, characterizing the nature and extent of repeat expansions, and understanding how these aberrant sequences contribute to pathogenesis at the molecular level.

Keywords: trinucleotide repeat, CAG repeat, expansion, gene, locus, cloning.

The discovery that SCA2 is caused by pathological expansion of CAG repeats in ATXN2 represented a critical milestone, firmly establishing the disease as a monogenic neurodegenerative disorder. Methodological approaches during this phase included gene mapping, molecular cloning, and the characterization of repeat instability, all aimed at clarifying the genetic architecture of SCA2. These foundational insights provided a genetic framework upon which subsequent studies —focused on neurodegeneration, biomarker development, and therapeutic strategies— would be built.

Implications: The outcomes of this stage laid the groundwork for a paradigm shift in SCA2 research. By establishing a definitive genetic cause, this period enabled a transition from descriptive pathology to mechanistic inquiry, opening avenues for translational research and targeted clinical applications in the following years. Furthermore, these findings positioned Cuban researchers within the global discourse on trinucleotide repeat disorders, fostering international collaborations and methodological innovation.

Stage 2010–2015: Pathophysiology and Disease Mechanisms (Teal to Green Nodes)

Between 2010 and 2015, research on SCA2 in Cuba progressed beyond genetic characterization to examine the neurobiological consequences of CAG repeat expansions. This phase marked a shift toward elucidating the pathophysiological mechanisms underlying disease progression, with a particular emphasis on brainstem and cerebellar dysfunction recognized as core contributors to the SCA2 phenotype. Research during this period focused on how the molecular consequences of *ATXN2* mutations give rise to cellular stress, neurodegeneration, and ultimately structural atrophy in specific brain regions.

Keywords: atrophy, brainstem, dysfunction, dominant cerebellar-ataxia.

Studies increasingly investigated the patterns and extent of cerebellar and brainstem atrophy, establishing these changes as hallmark indicators of disease manifestation and progression. This line of inquiry positioned dominant cerebellar ataxia not only as a clinical descriptor but also as a pathophysiological construct rooted in observable neuroanatomical changes. The integration of neuroimaging techniques and neuropathological analyses allowed researchers to draw direct links between genetic mutations and functional impairments in motor coordination, balance, and ocular movement control.

Implications: This research phase was pivotal in mapping the biological cascade from genotype to phenotype. By clarifying how genetic disruptions lead to localized brain degeneration, Cuban researchers laid a critical foundation for the design of longitudinal studies and clinical trials. Moreover, the emphasis on regional brain dysfunction provided a framework for identifying imaging biomarkers and evaluating therapeutic interventions aimed at slowing or halting neurodegeneration in SCA2.

Stage 2015-2020 (Clinical and Symptomatic Studies)-Green to Yellow Nodes

Between 2015 and 2020, Cuban research on SCA2 underwent a significant transition toward clinical and symptomatic investigation, marking a maturation of the research agenda from foundational science to translational application. This phase emphasized the identification of early clinical features, disease onset parameters, and measurable indicators of progression most notably saccade velocity, a reliable biomarker of oculomotor dysfunction in SCA2. The speed and accuracy of saccadic eye movements, which are characteristically impaired in SCA2 patients, emerged as a clinically sensitive and non-invasive tool for monitoring disease trajectory.

Keywords: clinical features, saccade velocity, age, motor, onset, early features.

Research during this period focused on refining the phenotypic characterization of SCA2, particularly through detailed assessments of motor symptoms, age at onset, and prodromal indicators. Attention was directed toward identifying clinical signs that precede overt ataxia, thereby enabling earlier diagnosis and intervention. This shift reflected a growing commitment to patient-centered research, in which previous discoveries in genetics and neurodegeneration were translated into clinically actionable insights.

Implications: The growing emphasis on clinical biomarkers and symptomatic profiling represents a critical evolution in the Cuban research landscape. By operationalizing concepts such as saccade velocity and early motor dysfunction, investigators not only advanced diagnostic precision but also laid the groundwork for stratified therapeutic strategies and longitudinal monitoring protocols. This period thus marks the integration of genetic and pathophysiological knowledge into real-world clinical practice, strengthening the interface between research and healthcare delivery for individuals affected by SCA2.

Co-Author Collaboration Network in Cuban Spinocerebellar Ataxia Type 2 Research

Figure 2 presents the co-author collaboration network in SCA2 research in Cuba between 2012 and 2020, capturing the structural and temporal dynamics of scientific collaboration within this field. The visualization maps key researchers, collaborative clusters, and evolving research priorities over time. Node size denotes the relative prominence of each author based on co-authorship frequency, with Luis Velázquez-Pérez and Roberto Rodríguez-Labrada emerging as central figures who have consistently facilitated collaboration across institutional and disciplinary boundaries. The network also highlights the integration of international collaborators, notably Georg Auburger and Ulf Ziemann, reflecting the increasingly global dimension of Cuban SCA2 research.

The color gradient applied to nodes —from dark blue (representing earlier collaborations circa 2012) to bright yellow (indicating more recent activity in 2020)— enables temporal analysis of research evolution. Early collaborations (2012–

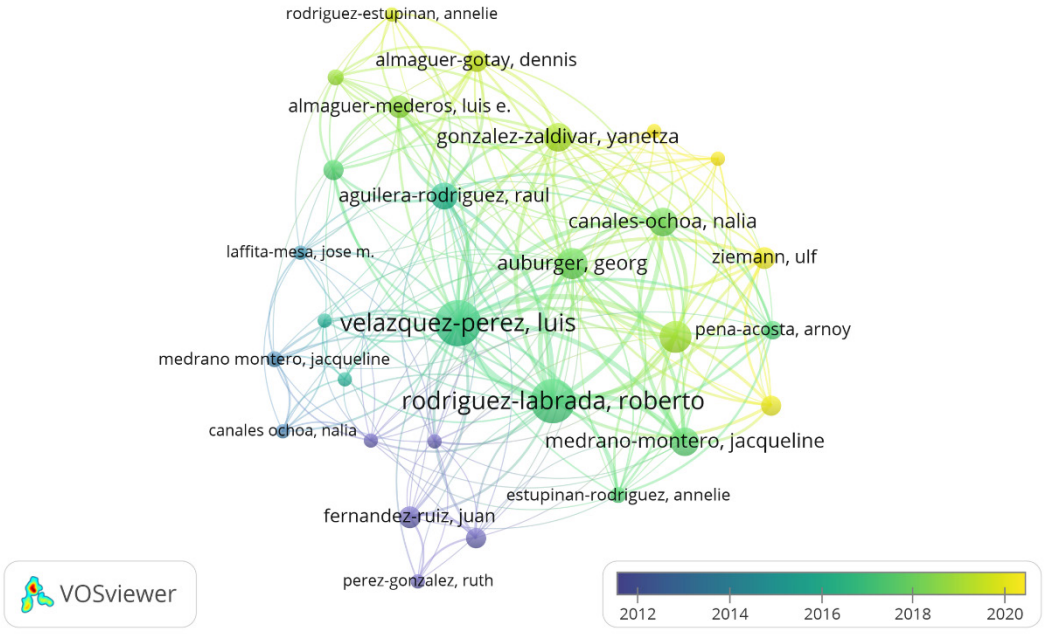

Fig. 2. Co-Author Collaboration Network in Cuban SCA2 Research (2012-2020): Authors with Contributions to Multiple Publications (> 3)

2014) were primarily centered on genetic characterization and clinical phenotyping, while more recent partnerships (2018-2020) have expanded to include biomarker development, diagnostic refinement, and translational research. This temporal layering reveals not only shifts in thematic focus but also the expansion and densification of the collaborative network over time.

Key Components of the Network Structure

Nodes (Authors): Each node represents an individual author active in Cuban SCA2 research. Node size is proportional to the author's centrality in the network, indicating a higher volume of collaborative activity. Color Coding (Timeline): Nodes are colored according to the period in which authors were most active. Dark blue indicates earlier activity (~2012), transitioning to bright yellow for recent collaborations (~2020), thus enabling a chronological interpretation of the network's development. Edges (Collaborations): The connecting lines (edges) represent co-authorship ties. Thicker lines indicate stronger collaboration intensity, reflecting repeated co-authorships or participation in multiple joint publications.

This co-authorship network underscores the structured growth, interdisciplinary expansion, and increasing internationalization of SCA2 research in Cuba. It demonstrates how core scientific leadership, sustained collaboration, and cross-border partnerships have collectively contributed to the consolidation of a robust research ecosystem focused on both the molecular and clinical dimensions of SCA2.

Analysis of Key Collaborators and Clusters

The co-authorship network in Cuban SCA2 research, as illustrated in figure 2, reveals a structured and evolving collaborative landscape between 2012 and 2020. At the center of this network are Luis Velázquez-Pérez and Roberto Rodríguez-Labrada, whose prominent node sizes and central positions indicate their sustained leadership and coordination roles. Their extensive collaborations across time periods suggest they act as key facilitators, linking multiple research groups and shaping the scientific direction of the field.

Two major collaborative clusters are identifiable in figure 2. The first, located on the left side of the visualization and associated with the 2012-2014 period, includes researchers such as Jose M. Laffita-Mesa, Jacqueline Medrano Montero, and Annelie Estupiñan Rodriguez. This group appears to have been involved in foundational studies focused on the genetic and early clinical characterization of SCA2.

In contrast, the second cluster, positioned on the right side of the figure and associated with more recent activity (2018–2020), features researchers such as Yanetz González-Zaldívar, Nalia Canales-Ochoa, Ulf Ziemann, and Georg

Auburger. This cluster is more densely connected and closely linked to the central authors, indicating active participation in current research initiatives that likely focus on clinical applications, biomarker development, and translational studies.

The inclusion of international collaborators such as Georg Auburger and Ulf Ziemann also stands out in figure 2. Their integration into the network highlights Cuba's increasing engagement with the global SCA2 research community. These links suggest collaborations that are not only strategic but also mutually beneficial, involving methodological exchange and broader research capacities.

Temporally, figure 2 reflects three distinct phases. From 2012 to 2014, collaborations were concentrated in a smaller group of researchers conducting genetic and epidemiological studies, which established the empirical foundation of SCA2 research in Cuba.

The period between 2015 and 2018 marks a phase of expansion and diversification, during which Velázquez-Pérez and Rodríguez-Labrada consolidated their positions as central figures, enabling broader interdisciplinary work across genetics, clinical neuroscience, and neurophysiology. Finally, from 2018 to 2020, the network becomes denser and more internationally oriented, with an intensified focus on patient-centered research, particularly the identification of clinical biomarkers and the development of diagnostic and therapeutic strategies. Overall, figure 2 illustrates how Cuban SCA2 research has evolved from its foundational genetic studies into a mature, translational, and globally connected scientific enterprise.

Institutional Collaboration Network in Cuban-Led Spinocerebellar Ataxia Type 2 Research

The institutional collaboration network in Cuban-led Spinocerebellar SCA2 research, as shown in figure 3, illustrates the structural composition and evolution of cooperative relationships between Cuban research centers and their international partners from 2010 to 2020. Each node in the network represents a participating institution, with its size proportional to its prominence in collaborative activities. The color gradient, ranging from dark blue (2010) to bright yellow (2020), enables temporal interpretation of institutional activity within the network.

Figure 3 highlights the Center for Research and Rehabilitation of Hereditary Ataxias (CIRAH) as the most central and influential institution in the network. As the largest node, CIRAH occupies a pivotal position in both national and international collaborations, indicating its role as a coordination hub for SCA2 research. Its consistent connectivity with multiple institutions underscores its strategic importance in facilitating interdisciplinary projects and knowledge transfer.

In close collaboration with CIRAH, other Cuban institutions such as the Cuban Academy of Sciences and the Cuban Center for Neurosciences also occupy central positions in the network. These institutions are actively engaged in linking clinical, neurological, and scientific approaches, reflecting the multidisciplinary character of SCA2 research in Cuba. Their interactions suggest an integrated research model where genetics, clinical neurology, and epidemiology converge.

International collaboration is a defining feature of this network. The University of Tübingen (Germany) shows a strong and longstanding partnership with CIRAH, likely focused on genetic and neurophysiological studies. Other German institutions —Goethe University Frankfurt, University of Ulm, and RWTH Aachen University— also maintain close ties with Cuban partners, contributing scientific expertise, infrastructure, and methodological rigor to the field.

Regional cooperation is represented by the National Autonomous University of Mexico (UNAM), which has established significant collaborative links with Cuban institutions. This partnership likely enables population-specific studies within Latin America, addressing genetic variability, clinical phenotypes, and environmental factors unique to the region. Such collaborations reflect a commitment to regional integration and knowledge co-production in the study of SCA2.

The network also demonstrates temporal trends in institutional participation. From 2010 to 2014, collaborations were primarily concentrated between CIRAH and German institutions, forming the foundation for early genetic and clinical investigations. The 2015-2017 period marks a phase of expansion, with the inclusion of Latin American partners such as UNAM, pointing to growing regional engagement and research diversification. In 2018-2020, new institutions such as the University of Holguín appear, while connections with European partners persist. This period indicates a possible shift toward applied research, including biomarker identification and diagnostic tool development.

Although not fully captured in figure 3, emerging collaborations with Australian and Japanese institutions in recent years may point to Cuba's involvement in international clinical trials and biomarker validation studies. These prospective alliances suggest an expanding research agenda that integrates foundational and translational efforts.

In summary, figure 3 reveals that CIRAH functions as the core institutional hub of Cuban-led SCA2 research, effectively linking national and international partners across a decade of scientific development. The sustained involvement of German institutions highlights a deep and productive collaboration, while the integration of Latin American partners such as UNAM reflects a strategic emphasis on regional priorities. The

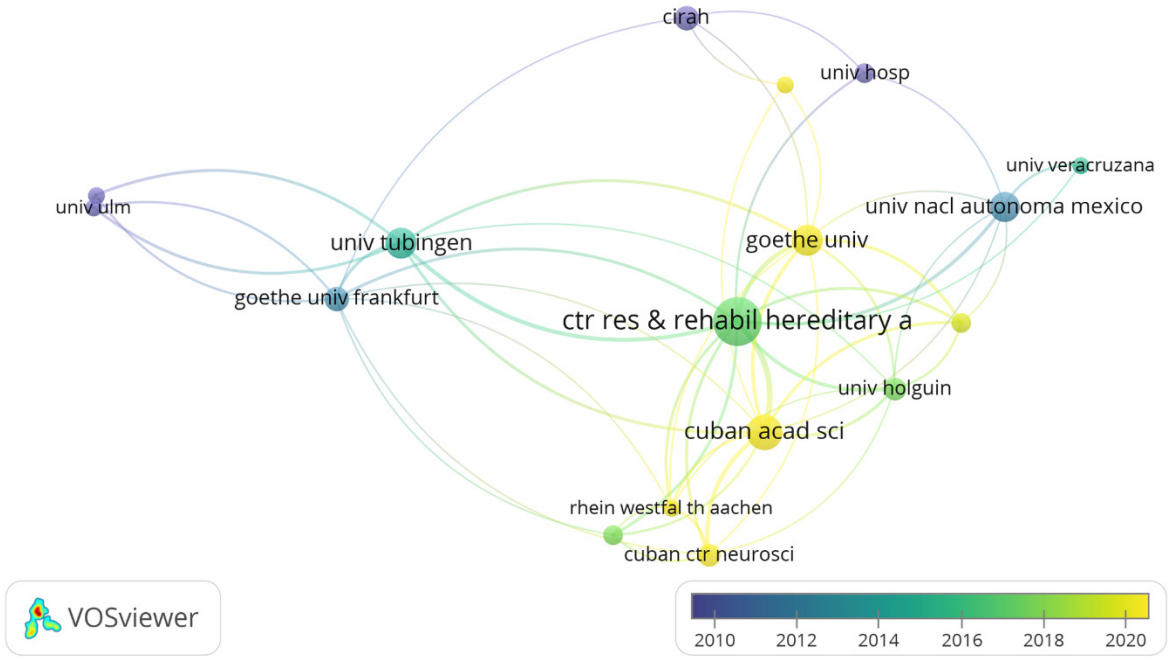

Fig. 3. Institutional Collaboration Network in Cuban SCA2 Research. Institutions with Contributions to Multiple Publications (> 5)

recent diversification of institutional participants suggests a dynamic and evolving research environment, oriented increasingly toward clinical translation and patient-centered applications. This co-institutional network exemplifies how Cuba has leveraged both long-standing international partnerships and regional alliances to build a robust and globally relevant research program in SCA2.

Global Collaboration Network of Cuban-Led Research in Spinocerebellar Ataxia Type 2

The global collaboration network in Cuban-led SCA2 research, as illustrated in figure 4, visualizes the international partnerships established between Cuba and various countries over a 15-year period, from 2005 to 2020. Constructed using VOSviewer, the network captures the evolution, intensity, and geographical diversity of these collaborations. Each node represents a country engaged in joint SCA2 research with Cuba, with node size reflecting the volume and prominence of the collaborative output. The color gradient —from dark blue (earlier years) to yellow (more recent activity)— allows for temporal interpretation of each country's involvement.

As expected, Cuba occupies the central position in the network, serving as the primary hub of coordination and research activity. Countries with the strongest ties to Cuba, such as Germany and Mexico, are represented by relatively large nodes and thick connecting lines, indicating long-standing and substantial collaborative relationships. These early partnerships, particularly active between 2005 and 2010, likely supported foundational studies in genetic etiology and initial clinical characterization of SCA2.

The network also shows a clear temporal progression in the diversification of partners. During the 2005-2010 period, collaboration was concentrated with Mexico and Germany—countries that provided both geographic proximity (in the case of Mexico) and scientific infrastructure (in the case of Germany). These early alliances were instrumental in establishing Cuba's research trajectory in the field, particularly regarding molecular genetics and epidemiological insights.

Between 2011 and 2015, the collaboration network expanded to include new partners such as the United States and Slovakia, as indicated by teal-colored connections. These additions suggest growing international recognition of Cuban contributions and may reflect efforts to incorporate advanced research technologies and diverse methodological frameworks. Notably, the involvement of U.S. institutions could have introduced novel expertise in neuroimaging, biomarker development, or computational modeling.

From 2016 to 2020, more recent collaborators such as Spain, Japan, and Australia entered the network, represented by yellow and light green nodes. These newer partnerships appear to emphasize translational and clinical dimensions of SCA2 research, including biomarker validation, therapeutic

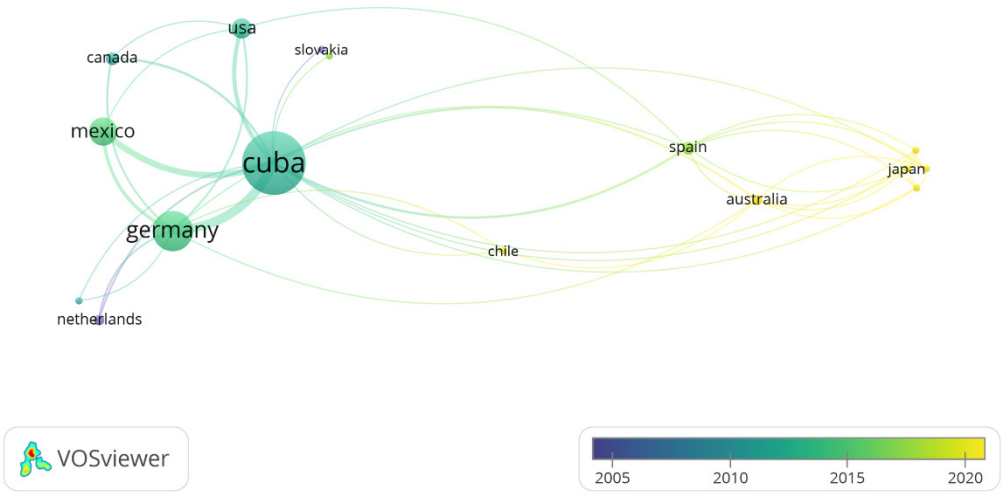

Fig. 4. International Collaboration Network in Cuban SCA2 Research (2005-2020). Countries with Contributions to Multiple Publications (> 2)

targeting, and patient-focused diagnostic tools. The emergence of Japan and Australia in this period signals an expansion of Cuba's scientific engagement across multiple continents and highlights the field's increasing global relevance.

The collaborative ties with Germany and Mexico remain prominent throughout the entire period, pointing to consistent alignment in research priorities and sustained institutional commitment. These relationships likely reflect shared goals in unraveling genetic underpinnings, developing clinical assessment tools, and co-authoring high-impact publications.

More recent alliances with Spain, Japan, and Australia appear to reflect a strategic shift in the Cuban research agenda toward applied and clinical investigations. These countries may contribute specialized capabilities in neurology, neurodegenerative disease management, and therapeutic trials, thereby complementing Cuba's existing strengths in genetic epidemiology and longitudinal patient studies.

Overall, figure 4 highlights the strategic nature of Cuba's international collaborations in SCA2 research, linking expertise from Latin America, Europe, North America, and Asia. This globally distributed network enhances the depth and breadth of research by enabling the exchange of diverse methodologies, access to broader patient populations, and the co-development of innovative research tools.

In summary, the collaborative trends shown in figure 4 can be delineated across three key periods: 2005-2010, dominated by foundational genetic research with Mexico and Germany; 2011-2015, marked by diversification into new regions such as the USA and Slovakia; and 2016-2020, characterized by the emergence of translational research partnerships with Spain, Japan, and Australia. These evolving dynamics illustrate how Cuban-led SCA2 research has progressively expanded its international footprint, moving from early-stage discovery science to complex, multi-site clinical applications.

DISCUSSION

This study examined the thematic evolution of SCA2 research in Cuba, highlighting thematic trends, key collaborative networks, and the evolution of research priorities from 1996 to 2024

The thematic network (see figure 1) reveals a shift from early genetic investigations to more clinically oriented research. Between 2005 and 2010, studies focused on the genetic basis of SCA2, particularly the role of *CAG* trinucleotide repeat expansions in the *ATXN2* gene (1, 3, 4), laying the foundation for future molecular and clinical exploration.

Advancements in molecular genetics led to the implementation of presymptomatic testing (PST) and prenatal diagnosis (PND) protocols in Cuba-home to the highest global prevalence of SCA2 and a substantial at-risk population. [4,26,27,28] In response, health professionals developed a multidisciplinary program involving neurologists, geneticists, psychologists, and primary care providers, reaching over 1,000 individuals. Notably, the Cuban PND program has served nearly 100 couples, with a 77.5% acceptance rate, offering reproductive choices in the absence of preimplantation genetic diagnosis. [22, 29,30,31]

From 2010 to 2015, research expanded to neurodegenerative mechanisms, incorporating terms like *brainstem*, *atrophy*, and *dysfunction*. This phase reflected efforts to understand the pathological impact of mutant *ATXN2* on cerebellar and

brainstem structures. By 2015-2020, the focus shifted toward prodromal detection and clinical monitoring, with increased attention to *saccade velocity*, *motor symptoms*, and *clinical features*, signaling a move toward translational research and patient-centered applications.

The collaboration networks (see figures 2 and 3) highlight the pivotal role of the Center for Research and Rehabilitation of Hereditary Ataxias (CIRAH), alongside the Cuban Academy of Sciences and the Cuban Center for Neurosciences, in coordinating national and international research. Long-standing partnerships with German institutions —such as the University of Tübingen, Goethe University Frankfurt, and University of Ulm— enabled Cuban researchers to build foundational expertise in genetic and clinical research.

Increasing collaboration with the National Autonomous University of Mexico (UNAM) suggests a growing emphasis on region-specific studies within Latin America, where SCA2 exhibits distinct genetic and phenotypic profiles. Recent alliances with institutions like the University of Holguín and European centers (e.g., Rheinische Westfälische Technische Hochschule Aachen) indicate a shift toward applied research, including biomarker development and therapeutic strategies. This diversification reflects the field's progression from basic genetic discovery to the development of diagnostic tools and interventions aimed at improving clinical outcomes for individuals affected by SCA2.

Conclusions

The analysis of SCA2 research themes and collaboration networks reveals a structured, evolving approach to SCA2 research in Cuba, with Cuban institutions not only leading regional studies but also integrating international expertise. CIRAH, along with other Cuban institutions, has played a central role in coordinating this research, establishing robust partnerships with German institutions and fostering regional collaborations within Latin America. The evolution of research topics from genetic underpinnings to clinical markers demonstrates a thoughtful progression toward translational research, underscoring Cuba's commitment to both scientific discovery and patient care.

The findings suggest that Cuban-led SCA2 research has transitioned from understanding the genetic basis of the disease to developing clinical tools for diagnosis and monitoring. Continued collaboration, especially with institutions specializing in clinical and translational research, will be essential to maintain this momentum and enhance the impact of SCA2 research on patient care.

In conclusion, Cuba's collaborative and thematic evolution in SCA2 research exemplifies an effective model of integrating foundational research with clinical applications through international and regional partnerships. By bridging genetic studies with clinical applications, Cuban researchers are laying the groundwork for more effective interventions and patient management strategies, ultimately aiming to improve quality of life for those affected by SCA2 in Cuba and beyond. Future research should continue to leverage these partnerships, focusing on applied research that translates genetic and pathophysiological insights into targeted therapies and diagnostics.

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