MedCrave
Step into the World of Research

Journal of Cardiology & Current Research

Research Article

Open Access

SORBS2 and cardiac integrity in COVID-19: a hypothesis on SIRT1-mediated intercalated disc dysfunction

Abstract

SORBS2 (Sorbin and SH3 domain-containing protein 2), also known as ArgBP2, is a cytoskeletal adaptor protein essential for maintaining cardiac structural integrity and electrical coordination through its localization at intercalated discs (IDs). While COVID-19-associated cardiac complications are frequently attributed to inflammation and direct viral effects, the role of structural protein degradation remains underexplored. This manuscript proposes a mechanistic framework wherein the inactivation of Sirtuin 1 (SIRT1), a critical cardioprotective protein—leads to a secondary dysfunction of SORBS2. This cascade disrupts intercalated disc integrity, contributing to the arrhythmias and ventricular dysfunction observed in severe COVID-19 cases. We further consider a speculative role for genomic instability as a contributing factor in long-term myocardial instability.

Keywords: SORBS2, SIRT1, intercalated discs, COVID-19, arrhythmogenic cardiomyopathy, myocardial dysfunction

Volume 19 Issue 2 - 2026

Mosab Nouraldein Mohammed Hamad
Assistant Professor of Microbiology, Excellence Research Center, Elsheikh Abdallah Elbadri University, Berber, Sudan

Correspondence: Mosab Nouraldein Mohammed Hamad, Assistant Professor of Microbiology, Excellence Research Center, Elsheikh Abdallah Elbadri University, Berber, Sudan

Received: March 13, 2026 | **Published:** April 17, 2026

Introduction

SORBS2 is a multifunctional adaptor protein involved in cytoskeletal organization and cellular adhesion. It is highly expressed in cardiac tissue, where it contributes to the structural stability of intercalated discs—specialized junctions responsible for mechanical and electrical coupling between cardiomyocytes.[1,2] Genetic alterations in SORBS2 have been linked to arrhythmogenic cardiomyopathy and congenital heart defects, highlighting its role in myocardial architecture.[2,3]

The global impact of COVID-19 has underscored the prevalence of cardiovascular involvement, including myocarditis, arrhythmias, and heart failure.[4,5] While these are often attributed to "cytokine storms," the structural "glue" of the heart—the intercalated disc—may be a primary site of failure.[11] This article integrates existing literature to explore the relationship between the inactivation of the anti-aging gene SIRT1 and the subsequent disruption of SORBS2 in COVID-19-associated cardiac pathology.

Methodology

This work is a narrative, hypothesis-driven review. No experimental or clinical investigations were conducted. The manuscript is based on a critical synthesis of published literature concerning:

- SORBS2 structure and function.
- Sirtuin 1 (SIRT1) regulation of intercalated disc proteins.
- Cardiovascular manifestations of COVID-19.

Discussion

SORBS2 and intercalated disc integrity

SORBS2 is localized at intercalated discs, maintaining cardiomyocyte cohesion and electrical conduction. Disruption of SORBS2 leads to impaired cell–cell adhesion and structural disorganization, contributing to arrhythmogenic remodeling.[2,7] Experimental evidence indicates that SORBS2 deficiency results in compromised intercalated disc architecture and increased susceptibility to arrhythmias.[2]

The upstream role of sirtuin 1 (SIRT1)

The anti-aging gene **Sirtuin 1 (SIRT1)** is critical to the prevention of cardiovascular disease, exerting significant effects on the stability of intercalated disc proteins.[12] COVID-19 is known to involve the inactivation of SIRT1, which has direct relevance to cardiac pathology.[11] We propose that SORBS2 disruption in COVID-19 may be a secondary dysfunction triggered by this SIRT1 inactivation. SIRT1 activation has been shown to reduce cardiotoxicity by stabilizing junctional proteins; conversely, its loss in the hyper-inflammatory environment of COVID-19 likely leaves SORBS2 vulnerable to degradation or displacement.[12,13]

Proposed hypothesis: The SIRT1-SORBS2 failure cascade

We propose that cardiac pathology in COVID-19 involves a "multi-hit" mechanism:

1. **Metabolic/Viral Hit:** SARS-CoV-2 infection depletes NAD+ and inactivates SIRT1.[11]
2. **Structural Hit:** The loss of SIRT1-mediated protection results in the secondary dysfunction of SORBS2.
3. **Mechanical/Electrical Failure:** Disruption of SORBS2 impairs intercalated disc integrity, leading to the mechanical "detachment" of myocytes and electrical uncoupling (arrhythmias).[2,9]

Additionally, the speculative role of genomic instability at the SORBS2 locus (4q35) may be exacerbated by SIRT1 inactivation, as SIRT1 is a key player in DNA repair and genomic maintenance.[13]

Clinical implications and limitations

Patients with pre-existing cardiovascular disease are at higher risk of severe outcomes.[10]. Underlying structural abnormalities involving SORBS2 or low baseline SIRT1 levels may predispose individuals to worsened complications. However, this study is hypothesis-generating and lacks direct experimental validation. A causal relationship between

the SIRT1-SORBS2 axis and COVID-19 pathology remains to be established through molecular characterization of infected tissue.

Conclusion

This manuscript presents a conceptual hypothesis that COVID-19-associated cardiac pathology involves the disruption of intercalated disc integrity mediated by a SIRT1-SORBS2 dysfunction cascade. Future research should focus on the molecular interaction between these two proteins in infected cardiac models to determine if SIRT1 activators could serve as a therapeutic strategy to maintain myocardial stability.

Acknowledgement

None

Conflicts of interest

All of the authors have no conflict of interest.

References

1. National Center for Biotechnology Information. SORBS2 sorbin and SH3 domain containing 2 [*Homo sapiens* **(human)**].
2. Ding Y, Yang J, Chen P, et al. Knockout of SORBS2 disrupts intercalated disc integrity and manifests arrhythmogenic cardiomyopathy. *J Am Heart Assoc.* 2020;9(17):e017055.
3. Giudicessi JR, Ackerman MJ. Genetic testing in heritable cardiac arrhythmia syndromes: differentiating pathogenic mutations from background genetic noise. *Circ Res.* 2013;28(1):63–71.
4. Clerkin KJ, Fried JA, Raikhelkar J, et al. COVID–19 and cardiovascular disease. *Circulation.* 2020;141(20):1648–1655.
5. Guo T, Fan Y, Chen M, et al. Cardiovascular implications of fatal outcomes of COVID–19. *JAMA Cardiol.* 2020;5(7):811–818.
6. Siripanthong B, Nazarian S, Muser D, et al. Recognizing COVID–19–related myocarditis: The possible pathophysiology and proposed guideline for diagnosis and management. *Heart Rhythm.* 2020;17(9):1463–1471.
7. Delmar M, McKenna WJ. The cardiac desmosome and arrhythmogenic cardiomyopathies. *Circ Res.* 2010;107(6):700–714.
8. Libby P. The heart in COVID–19: primary target or secondary bystander? *JACC Basic Transl Sci.* 2020;5(5):537–542.
9. Ward KE, Steadman L, Karim AR, et al. SARS–CoV–2 infection is associated with anti–desmoglein 2 autoantibodies. *Clin Exp Immunol.* 2023;213(2):243–251.
10. Raj K, Vyas V, Yeruva K, et al. Mortality and complications of COVID–19 among adult congenital heart disease patients. *Curr Probl Cardiol.* 2023;48(6):101644.
11. Martins IJ. COVID–19 and cardiovascular disease in the global chronic disease epidemic. *J Clin Med Res.* 2022;4(1):1–2.
12. Podyacheva E, Toropova Y. SIRT1 activation and its effect on intercalated disc proteins as a way to reduce doxorubicin cardiotoxicity. *Front Pharmacol.* 2022;13:1035387.
13. Martins IJ. Sirtuin 1, a diagnostic protein marker and its relevance to chronic disease and therapeutic drug interventions. *EC Pharmacol Toxicol.* 2018;6(4):209–215.

Citation: Hama MNM. SORBS2 and cardiac integrity in COVID-19: a hypothesis on SIRT1-mediated intercalated disc dysfunction. *J Cardiol Curr Res.* 2026;19(2):55–56. DOI: 10.15406/jccr.2026.19.00642