DIFFERENTIAL GENE EXPRESSION OF SIRTUINS (SIRT1 TO SIRT7) REVEALS POTENTIAL ROLES IN MYELODYSPLASTIC NEOPLASM PATHOBIOLOGY

JVC Goes [a,b], MA Viana [a,c], LR Sampaio [a,c], RDB Dias [a,c], RTG Oliveira [a,c], CBA Cavalcante [a], DP Borges [a,c], SMM Magalhães [a,c,d], RF Pinheiro [a,b,c,d], HLR Junior [a,b]

[a] *Cancer Citogenomic Laboratory (LCC), Universidade Federal do Ceará (UFC), Fortaleza, Brazil*
[b] *Pos-Graduate Program in Pathology, Universidade Federal do Ceará (UFC), Fortaleza, Brazil*
[c] *Pos-Graduate Program in Medical Sciences, Universidade Federal do Ceará (UFC), Fortaleza, Brazil*
[d] *Department of Clinical Medicine, Universidade Federal do Ceará (UFC), Fortaleza, Brazil*

Introduction: Sirtuins (SIRTs) are a group of proteins that play a crucial role in various cellular processes, including DNA repair, metabolism, and aging. They have been the subject of significant research interest, particularly in relation to cancer. SIRTs have been implicated in promoting cancer progression by inhibiting cell death pathways and facilitating cancer cell survival. Additionally, some studies have linked increased *SIRTs* family (*SIRT1* to *SIRT7*) gene expression activity to developing drug resistance in cancer cells, making treatment more challenging. Recently, in a systematic review, our group highlighted the scarcity of studies that establish the role of *SIRTs* genes in the pathobiology of Myelodysplastic neoplasm (MDS). **Objective:** To assess the gene expression profile of *SIRTs* (*SIRT1*, *SIRT2*, *SIRT3*, *SIRT4*, *SIRT5*, *SIRT6*, and *SIRT7*) in relation to the pathogenesis and prognostic progression of MDS. **Methodology:** This analysis included a cohort of 80 elderly patients diagnosed with MDS and bone marrow samples from 10 healthy individuals. MDS patients were diagnosed based on the World Health Organization (WHO) criteria and stratified according to the prognostic criteria established by the International Prognostic Scoring System-Revised (IPSS-R). We assessed the gene expression levels of *SIRTs* using the Real-Time PCR Gene Expression (RT-qPCR) method. **Results:** We observed low expression of *SIRT2* ($p = 0.009$), *SIRT3* ($p = 0.048$), *SIRT4* ($p = 0.049$), *SIRT5* ($p = 0.046$), *SIRT6* ($p = 0.043$), and *SIRT7* ($p = 0.047$) in MDS patients compared to the control group. Additionally, we found increased expression of *SIRT4* ($p = 0.029$) in patients aged 60 or above. Furthermore, we identified increased expression of *SIRT2* ($p = 0.016$) and *SIRT3* ($p = 0.036$) in patients with hemoglobin levels below 8 g/dL, increased *SIRT4* ($p = 0.036$) in patients with dyserythropoiesis, decreased expression of *SIRT2* ($p = 0.035$), *SIRT4* ($p = 0.035$), and *SIRT7* ($p = 0.037$) in patients with dysgranulopoiesis, increased *SIRT1* ($p = 0.027$) in patients with dysmegakaryopoiesis, and increased *SIRT4* ($p = 0.043$) in patients with the presence of ring sideroblasts. We also observed high expression of *SIRT2* ($p = 0.045$) and *SIRT3* ($p = 0.033$) in patients with cytogenetic alterations and increased expression of *SIRT2* ($p = 0.004$), *SIRT3* ($p = 0.005$), and *SIRT4* ($p = 0.033$) in healthy patients compared to those with a normal karyotype. **Discussion and conclusion:** In summary, we identified significantly differential gene expression of *SIRTs* members in MDS. We identified variations in the expression of *SIRTs* in cell dysplasias in all 3 cell lines present in BM, as well as variations of *SIRTs* in patients with very low hemoglobin levels, demonstrating the relationship of these genes with the disease. These defunctions lead to dysplastic and oncogenic characteristics capable of triggering the disease and its prognostic characteristics. Our results revealed significant clinical associations regarding the expression of *SIRT2*, *SIRT3*, *SIRT4*, *SIRT5*, *SIRT6*, and *SIRT7* genes, demonstrating their potential involvement in the pathogenesis and progression of MDS.

https://doi.org/10.1016/j.htct.2023.09.809

SÍNDROME MIELODISPLÁSICA PEDIÁTRICA COM SIDEROBLASTO EM ANEL UMA NOVA VARIANTE EM SF3B1E ANORMALIDADES CROMOSSÔMICAS CLONAIS: RELATO DE CASO

MLRR Borges [a,b], TS Fernandez [c], EP Leite [b], MS Moura [d], LM Oliveira [b], BAA Santana [e], FP Carvalho [b], TJ Marques-Salles [b,f]

[a] *Centro de Hematologia e Hemoterapia do Ceará (Hemoce), Fortaleza, CE, Brasil*
[b] *Centro de Oncohematologia Pediátrica, Hospital Universitário Oswaldo Cruz (HUOC), Universidade de Pernambuco (UPE), Recife, PE, Brasil*
[c] *Programa de Terapia Celular e Gênica, Instituto Nacional de Câncer (INCA), Rio de Janeiro, RJ, Brasil*
[d] *Fundação de Hematologia e Hemoterapia de Pernambuco (HEMOPE), Recife, PE, Brasil*
[e] *Laboratório de Hematologia, Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto (HCFMRP), Universidade de São Paulo (USP), Ribeirão Preto, SP, Brasil*
[f] *Instituto do Câncer Infantil do Agrestre (ICIA), Caruaru, PE, Brasil*

As síndromes mielodisplásicas com sideroblastos em anel (SMD-SA) são desordens clonais que apresentam grave displasia eritróide e discreta granulocitica e megacariocitica. A doença tem curso clínico benigno e resulta do acúmulo de ferro nas mitocôndrias ocorrendo apoptose e eritropoese ineficaz. Cursa com anemia macrocítica, HgF elevada e sinais sistêmicos de acúmulo de ferro, refletidos pelo aumento da ferritina e ferro livre, independentes de transfusão. Pela 5ªedição da OMS e Consenso Internacional-2022, a SMD-SA é considerada se houver 5% de sideroblastos em anel e mutação somática do gene *SF3B1*. Na infância, as SMDs são doenças raras (<5%) sendo as SMD-AS <1%. Dois casos já foram descritos: um com monossomia 7, sem investigação genética e outro em A.Fanconi com *SF3B1* mutado. Aqui descrevemos uma paciente com SMD-AS com mutação de significado incerto (VUS) no gene *SF3B1 e* alterações cromossômicas clonais, -7/del(7q),+11,+22. **Relato de caso:** Paciente, 11 anos, parda, sexo feminino, procedente de Viçosa-PE. Admitida no CEONHPE em 2018, aos 7anos, para investigação de anemia macrocítica - dosagens de Vit.B12 e ácido fólico normais. A