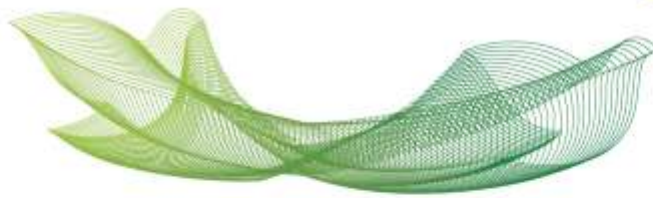




Tipo	Periódico
Título	Extent of rescue of F508del-CFTR function by VX-809 and VX-770 in human nasal epithelial cells correlates with SNP rs7512462 in SLC26A9 gene in F508del/F508del Cystic Fibrosis patients
Autores	Arthur Kmit, Fernando Augusto Lima Marson, Stéphanie Villa-Nova Pereira, Adriana Mendes Vinagre, Gabriela Silva Leite, Maria Fátima Servidoni, José Dirceu Ribeiro, Antônio Fernando Ribeiro, Carmen Sílvia Bertuzzo, Margarida Duarte Amaral
Autor (es) USF	Fernando Augusto Lima Marson
Autores Internacionais	Margarida Duarte Amaral
Programa/Curso (s)	Programa de Pós-Graduação Stricto Sensu em Ciências da Saúde
DOI	10.1016/j.bbadis.2019.01.029
Assunto (palavras chaves)	Cystic fibrosis; CFTR modulator drugs; CFTR; CRC-HNE; Modifier genes; SLC26A9; Ussing chamber
Idioma	Inglês
Fonte	Título do periódico: Biochimica Et Biophysica Acta. Molecular Basis Of Disease ISSN: 0925-4439 Volume/Número/Paginação/Ano: v. 1865, p. 1323-1331, 2019
Data da publicação	1 June 2019
Formato da produção	Vários https://doi.org/10.1016/j.bbadis.2019.01.029
Resumo	<p>Background: We analyzed the CFTR response to VX-809/VX-770 drugs in conditionally reprogrammed cells (CRC) of human nasal epithelium (HNE) from F508del/F508del patients based on SNP rs7512462 in the Solute Carrier Family 26, Member 9 (SLC26A9; MIM: 608481) gene.</p> <p>Methods: The Isc-eq measurements of primary nasal epithelial cells from F508del/F508del patients (n = 12) for CFTR function were performed in micro Ussing chambers and compared with non-CF controls (n = 2). Data were analyzed according to the rs7512462 genotype which were determined by real-time PCR.</p> <p>Results: The CRC-HNE cells from F508del/F508del patients evidenced high variability in the basal levels of CFTR function. Also, the rs7512462*C allele showed an increased basal CFTR function and higher responses to VX-809 + VX-770. The rs7512462*CC + CT genotypes together evidenced CFTR function levels of 14.89% relatively to wt/wt (rs7512462*CT alone-15.29%) i.e., almost double of rs7512462*TT (7.13%). Furthermore, sweat [Cl⁻] and body mass index of patients also evidenced an association with the rs7512462 genotype.</p> <p>Conclusion: The CFTR function can be performed in F508del/F508del patient-derived CRC-HNEs and its function and responses to VX-809 + VX-770 combination as well as</p>



	clinical data, are all associated with the rs7512462 variant, which partially sheds light on the generally inter-individual phenotypic variability and in personalized responses to CFTR modulator drugs.
Fomento	