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Título	Extensive CFTR sequencing through NGS in Brazilian individuals with cystic fibrosis: unravelling regional discrepancies in the country
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Resumo	Background: The Brazilian population has a tri-hybrid composition with a high degree of ethnic admixture. We hypothesized that Brazilian individuals with CF from different Brazilian regions have a specific distribution of CFTR variants. Methods: Individuals with CF with data available in the Patient Registry and without an established genotype were submitted to CFTR sequencing by Next Generation Sequencing (NGS) methodology, and results were anonymously incorporated to the Registry Database. Genotyping results were expressed as 'positive', 'inconclusive' or 'negative'. Logistic regression models were performed to investigate the association between demographic/clinical variables and genotyping results. Mediation analysis was conducted to estimate direct and indirect effects of Brazilian region on a binary positive genotyping response. Results: In October 2017, data from 4,654 individuals with CF were available, and 3,104(66.7%) of them had a genotyping result. A total of 236 variants (114 new variants) were identified, with F508del identified in 46% of the alleles tested. Genotyping revealed 2,002(64.5%) individuals positive, 757(24.4%) inconclusive and 345(11.1%) negative. Distribution of genotype categories was markedly different across Brazilian Regions, with greater proportions of negative individuals in the North (45%) and Northeast (26%) regions. Newborn screening (CF-NBS) and age at diagnosis were identified as mediators of the effect of Brazilian region on a positive genotyping result. Conclusions: This large initiative of CFTR genotyping showed significant regional discrepancies in Brazil, probably related to socio-economic conditions, lack of adequate CF-NBS and poor access to reliable sweat testing. These results may be useful to indicate Regions where CF care demands more attention.
Fomento	