Validation of a PCR-Based Protocol for FCGR3A V158F Polymorphism in MOGAD and NMOSD-AQP4+ Patients: Toward Personalized Rituximab Therapy

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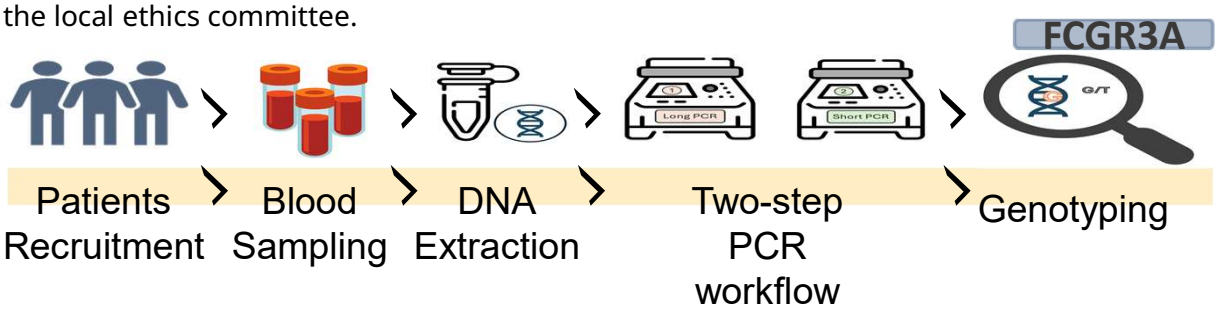
Aim: Rituximab efficacy varies among patients with autoimmune and hematologic conditions. The *FCGR3A* gene polymorphism rs396991 (G>T), leading to a V158F amino acid change in the FcγRIIIa receptor, influences its affinity for IgG1 antibodies and affects antibody-dependent cellular cytotoxicity (ADCC). The GG genotype (V/V phenotype) is associated with higher affinity and possibly greater clinical benefit.
We aimed to validate a genotyping protocol for *FCGR3A* V158F polymorphism in patients with Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease (MOGAD) and Neuromyelitis Optica Spectrum Disorder with Aquaporin-4 antibodies (NMOSD-AQP4+).

Patients: Seven patients (3 MOGAD, 4 NMOSD-AQP4+) followed at Fondazione Policlinico Universitario A. Gemelli IRCCS (Rome) were enrolled in a genetic testing study approved by the local ethics committee.



Methods: The PCR protocol for the *FCGR3A* gene was adapted from Mahaweni NM, et al. 2018. We used primers designed to discriminate this isoform from its homolog *FCGR3B* selectively. To achieve exclusive amplification of *FCGR3A*, a two-step PCR was performed. Initially, a long PCR was carried out to amplify only the isoform of interest. Subsequently, a short PCR was performed to amplify the region containing the targeted polymorphism. The product of the short PCR was then sequenced, allowing discrimination between the two isoforms and characterization of the V158F polymorphism in *FCGR3A*.

Patient	Disease	FCGR3A polymorphism	outcome
1	MOGAD	V/V	No relapse over four years
2	AQP4+	V/F	Relapser, switched to satralizumab
3	MOGAD	F/F	No relapse over three years
4	MOGAD	V/F	No relapse over three years
5	AQP4+	F/F	No relapse over two years
6	AQP4+	V/F	Relapser, switched to satralizumab
7	AQP4+	F/F	Relapser, switched to satralizumab

Discussion: The protocol was feasible and accurate. Preliminary results suggest *FCGR3A* V158F genotyping may help predict rituximab response in MOGAD and NMOSD-AQP4+, supporting personalized treatment approaches.

Conclusion: Genotyping *FCGR3A* V158F is feasible and may serve as a predictive biomarker in MOGAD and NMOSD-AQP4+ patients treated with rituximab.

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