gMS-Classifier1 does not predict disability progression in multiple sclerosis

Johannis A. van Rossum

*Vrije Universiteit Amsterdam*

*Et al.*

---

**Let us know how access to this document benefits you.**

Follow this and additional works at: [https://escholarship.umassmed.edu/oapubs](https://escholarship.umassmed.edu/oapubs)

Part of the Amino Acids, Peptides, and Proteins Commons, Biological Factors Commons, Immune System Diseases Commons, Nervous System Diseases Commons, and the Pathological Conditions, Signs and Symptoms Commons

---

**Repository Citation**


---

**Creative Commons License**

This work is licensed under a Creative Commons Attribution-Noncommercial 4.0 License

This material is brought to you by eScholarship@UMMS. It has been accepted for inclusion in Open Access Articles by an authorized administrator of eScholarship@UMMS. For more information, please contact Lisa.Palmer@umassmed.edu.
gMS-Classifier1 does not predict disability progression in multiple sclerosis

Date received: 24 July 2018; accepted: 9 August 2018

Several clinical, immunological and radiological biomarkers have been shown to predict the disease course of multiple sclerosis (MS).1–5 One potential serum marker is the gMS-Classifier1, which is composed of IgM anti-Glc antibodies, namely anti-GAGA 2,3,4 and 6. Previous work demonstrated that the gMS-Classifier1 could not predict early conversion to clinically definite MS in a cohort of clinically isolated syndrome (CIS) patients, but predicted Expanded Disability Status Scale (EDSS) progression. Significance, however, was dependent on covariates, and confirmation in an independent study was required.3

The aim of this study was to test if the gMS-Classifier1 could predict early disability progression in a large multicenter cohort of patients with CIS or relapse-onset MS.

Blood samples and clinical data were prospectively collected in four MS centers between 1993 and 2007: The Ottawa Hospital, Ottawa, Canada; Amsterdam University Medical Centers, the Netherlands; UMass Memorial Medical Center, Worcester, USA; and Hospital Ramón y Cajal, Madrid, Spain. Patients had a diagnosis of CIS (n=118) or relapsing remitting multiple sclerosis (RRMS; n=240) at study onset. Age at blood sampling was between 18 and 50 years. Serum samples were stored frozen < -70°C until assayed.

Baseline (EDSS) was performed within 6 months of blood sampling and was repeated during patient routine visits. Disability progression was defined as a sustained (≥6 months) progression of at least 1.0 EDSS point over the baseline EDSS and progression to an EDSS score of 3.0 or higher.

Mean follow-up was 94 months.

In 2012, frozen serum samples were shipped to Glycominds Inc Lab (Simi Valley, CA, USA) for testing for anti-glycan antibodies as described before.3 If one of the antibodies was above the predefined cut-off (anti-GAGA2 >148.8 EIA units, anti-GAGA3 >164.6 EIA units, anti-GAGA4 >133.6 EIA units, and anti-GAGA6 >168.1 EIA units), patients were considered positive for the gMS-Classifier1. There were no significant differences for the key variables gMS-Classifier1 and EDSS progression between the four centers.

Of the 358 patients, 44 (12.3%) were gMS-Classifier1 status positive. EDSS progression was available for 355 patients, of whom 158 (44.5%) had confirmed progression at the end of follow-up. The percentage of patients showing EDSS progression did not differ between the groups, using the 1 point EDSS progression definition (p=0.587) or for EDSS progression above 3.0 (p=0.771). There was no association between EDSS progression and the gMS-Classifier1 (p=0.778) or positive titres for any of the separate antibodies (anti-GAGA2: p=0.934, anti-GAGA3: p=0.663, anti-GAGA4: p=0.712, and anti-GAGA6: p=0.440).

No statistical differences between the gMS-Classifier1 positive and negative group were observed for age (p=0.631), disease duration (p=0.147), gender (p=0.154), baseline EDSS (p=1.000), number of CIS patients at blood sampling (p=0.865), follow-up time (p=0.587), relapse at blood sampling (p=0.771), and steroids at blood sampling (p=1.000).

Here, we present the results of a large cohort of patients from different centers from two continents, showing no statistical differences between gMS-Classifier1 positive and negative patients, convincingly indicating that the gMS-Classifier1 does not predict disability progression in MS.

Declaration of Conflicting Interests
The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Johannis A. van Rossum reports no conflicts of interest. Luisa M. Villar received payment for lecturing, travel expenses, research grants or consultancy from Merck-Serono, Biogen, Sanofi-Genzyme, Roche, and Novartis. Peter N. Riskind is a site principal investigator for clinical trials with Hoffman-Laroche/Genentech, Biogen, and the National Multiple Sclerosis Society. Mark S. Freedman received educational grants from Genzyme.
Canada, honoraria or consultation fees from Actelion, BayerHealthcare, BiogenIdec, Chugai, Clene Nanomedicine, EMD Canada, Genzyme, Merck Serono, Novartis, Hoffman La-Roche, Sanofi-Aventis, Teva Canada Innovation, is a member of a company advisory board, board of directors or other similar group for Actelion, BayerHealthcare, BiogenIdec, Clene Nanomedicine, Hoffman La-Roche, Merck Serono, MedDay, Novartis, Sanofi-Aventis and participates in a company sponsored speaker’s bureau of Sanofi-Genzyme. Charlotte Teunissen served on the advisory board of Fujirebio and Roche, received research consumables from Euroimmun, IBL, Fujirebio, Invitrogen, and Mesoscale Discovery, and performed contract research for IBL, Shire, Boehringer, Roche, and Probiodrug. Joep Killestein has accepted speaker and consultancy fees from Merck, Biogen, Teva, Genzyme, Roche and Novartis.

Funding
The author(s) declared receipt of the following financial support for the research, authorship, and/or publication of this article: Biomarker analysis for measurement of anti-glycan antibodies was funded and performed by Glycominds Incorporation.

ORCID iD
Johannis A van Rossum https://orcid.org/0000-0002-0996-012X

References

Johannis A van Rossum1, Joep Killestein1, Luisa M Villar2, Peter N Riskind3, Mark S Freedman4, and Charlotte Teunissen5
1Department of Neurology, Amsterdam Neuroscience, MS Center Amsterdam, VU University Medical Center Amsterdam, Amsterdam, The Netherlands
2Department of Neurology, Hospital Universitario Ramón y Cajal, Madrid, Spain
3Memorial Multiple Sclerosis Center, Department of Neurology, UMass Memorial Medical Center, Worcester, MA, USA
4Division of Neurology, Department of Medicine, University of Ottawa, The Ottawa Hospital Research Institute, Ottawa, ON, Canada
5Department of Clinical Chemistry, Amsterdam University Medical Centers, The Netherlands

Correspondence to:
JA van Rossum
Department of Neurology, Amsterdam Neuroscience, MS Center Amsterdam, VU University Medical Center Amsterdam, PO Box 7057, 1007 MB Amsterdam, The Netherlands.
j.vanrossum@vumc.nl

Analysis of Canadian multiple sclerosis patients does not support a role for FKBP6 in disease

Date received: 21 June 2018; accepted: 30 August 2018

We read with interest a recent article by Mescheriakova et al.1 entitled Linkage analysis and whole exome sequencing identify a novel candidate gene in a Dutch multiple sclerosis family. In this study, the authors described a missense variant in FKBP6 (p.R183C, rs147213094) co-segregating with multiple sclerosis (MS) in eight individuals from a large Dutch multi-incident family. Four healthy family members were also found to harbour this mutation, and it was not observed in one family member diagnosed with MS. Reduced penetrance and the presence of phenocopies does not detract from the authors’ claim as familial forms of complex diseases, including MS, are genetically heterogeneous.2–5 In addition, albeit not statistically significant,