Receptor activity modifying protein 1 (RAMP1) gene promoter methylation is associated with female migraine susceptibility

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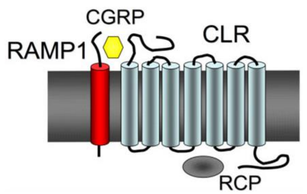
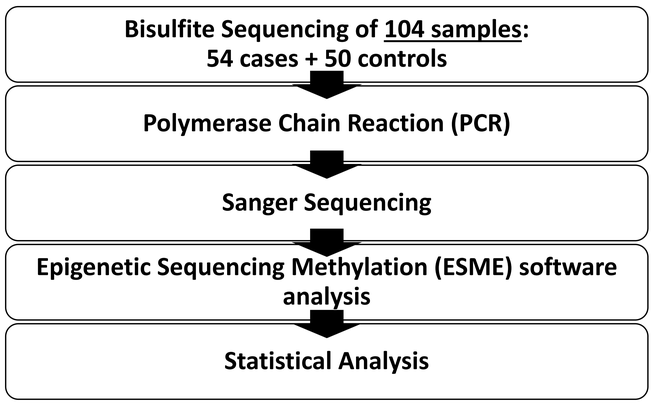
INTRODUCTION

Migraine is a complex debilitating neurovascular disorder characterized by attacks of moderate to severe headache pain lasting 4 to 72h and symptoms may include photophobia, phonophobia, nausea and vomiting.
Calcitonin Gene Related Peptide (**CGRP**) is frequently implicated in migraine pathophysiology and is a target for migraine treatment.
CGRP receptor consists of three proteins: Calcitonin Receptor-Like Receptor (**CLR**); Receptor Activity Modifying Protein 1 (**RAMP1**) and Receptor Component Protein (**RCP**).



DNA methylation occurs mostly at cytosine residues in CpG dinucleotides in the gene promoter. It can control gene expression by recruiting proteins involved in gene repression or by impeding the binding of transcription factors to DNA.

METHODS

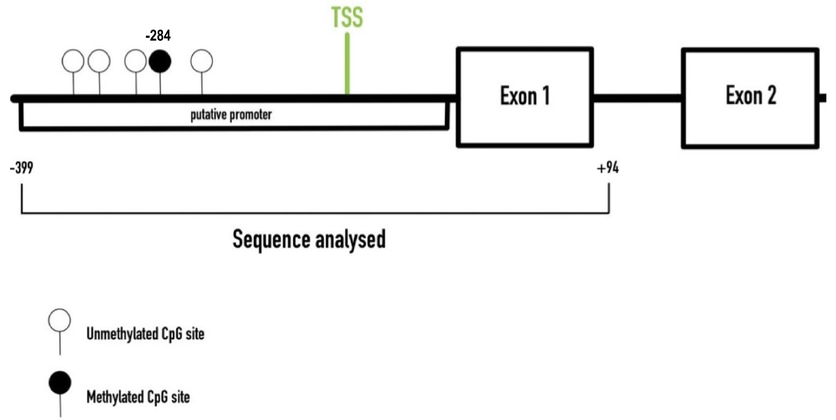


RESULTS

- **51 CpG** identified in our analysed sequence – only the first 5 showed variability
- Higher proportion of migraine cases with **all five CpG units methylated** compared to controls (26% vs 16%)
- **-284 CpG unit** (related to the Transcription Start Site) **showed significantly higher methylation** levels in cases when compared to controls

CpG UNIT	OR	95%C.I.	P-VALUE
-346	0.99	(0.95 - 1.03)	0.582
-334	1.02	(0.99 - 1.07)	0.509
-284	1.06	(1.01 - 1.12)	0.017*
-276	0.97	(0.92 - 1.02)	0.225
-234	0.98	(0.93 - 1.03)	0.411

OR- odds ratio; C.I.- confidence interval. *p<0.05



DISCUSSION

Only one study, relying on a small sample size, has analyzed the methylation of the human RAMP1 promoter in the context of migraine[1]. Our preliminary results seem to contradict that study as we found that **female migraineurs generally tend to have higher methylation levels** than female controls.

➢ **We discovered a new CpG unit potentially associated to migraine** which may disrupt the transcription of CGRP.

REFERENCES
1. Wan, D.; Hou, L.; Zhang, X.; Han, X.; Chen, M.; Tang, W.; Liu, R.; Dong, Z.; Yu, S. DNA methylation of RAMP1 gene in migraine: an exploratory analysis. The journal of headache and pain **2015**, 16, doi:10.1186/S10194-015-0576-7.

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