Evaluation of Novel Platelet Polymorphisms in Stroke.
Dichotomic Effect of rs5443 in GNB3

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Dear Editor,

Our group recently characterized two single-nucleotide polymorphisms (SNPs), rs4366150 and rs1787566, on the genes encoding lysophosphatidic acid receptor-1 (LPARI) and myosin VB (MYOSB), respectively, which are associated with platelet reactivity, in a cohort of 286 healthy children.1 Furthermore, the recently identified SNPs rs5443 (on the gene encoding guanine nucleotide binding protein 3, GNB3) and rs3737224 (on the gene encoding platelet endothelial aggregation receptor 1, PEAR1)2,3 may also be considered as potential new genetic factors implicated in platelet function. However, the role of these SNPs in thrombosis or hemorrhage disorders has either not been addressed, or is still controversial.

For this purpose, the presence of the four SNPs was determined in consecutive patients who survived an IS and in patients who suffered from an intracranial hemorrhage [subarachnoid hemorrhage (SAH) and intracerebral hemorrhage (ICH)].

For this study by segregating by gender. The results showed that while in women the T allele of rs5443 was not associated with IS (p=0.713), there was a statistically significant, almost three-fold increase in the risk of developing IS among men without
Table 1. Clinical features and prevalence of selected risk factors in case-control study

|                  | Controls (n=111) | IS (n=118) | p* | OR (95% CI) | SAH (n=102) | p* | OR (95% CI) | ICH (n=164) | p* | OR (95% CI) |
|------------------|-----------------|------------|----|-------------|-------------|----|------------|-------------|----|------------|
| Age [year]       |                 |            |    |             |             |    |            |             |    |            |
| Range            | 18-87           | 32-97      |    | -           | 19-90       | -  | 25-99      | -           |    |            |
| Mean±SD          | 48.6±19.6       | 73.3±12.3  | <0.001 | 59.6±12.6 <0.001 | -           | 69.6±4.7 | <0.001     | -           |    |            |
| Male sex (%)     | 54(±12.6)       | 46±12.6    | 0.012 | 39±0.012    | 66±0.012    | 66 | 0.0059     |             |    |            |
| Risk factors (%) |                 |            |    |             |             |    |            |             |    |            |
| Current/former smoker |       |            |    |             |             |    |            |             |    |            |
| Hypertension     | 21±68           | 42±0.025   | 0.0001 | 42±0.0001   | 67±0.001   | 67 | 0.001      |             |    |            |
| Dyslipidemia     | 12±37           | 37±<0.001  | -   | 65.2±0.012  | 65.2±0.012  | 32 | 0.593      |             |    |            |
| Diabetes mellitus| 9.5±45.7        | -          | 0.012 | -           | -           | -  |            | -           |    |            |
| PEAR1 rs3737224, n (%) | 138(22.7) | 28(23.7)  | 0.814 | 27(26.5) 0.409 | -           | 39(23.8) | 0.778     |             |    |            |
| LPAR1 rs4366150, n (%) | 387(45.3) | 77(65.3)  | 0.876 | 74(72.5) 0.115 | -           | 104(63.4) | 0.797     |             |    |            |
| MYO5B rs1787566, n (%) | 194(32.1) | 31(26.3)  | 0.215 | 28(27.1) 0.385 | -           | 49(29.9) | 0.593     |             |    |            |
| GNB3 rs5443, n (%) | 342(60.0) | 77(65.3)  | 0.087 | 48(47.1) 0.071 | -           | 95(57.9) | 0.781     |             |    |            |
| Total subjects   | 342(60.0)       | 77(65.3)  | 0.087 | 48(47.1) 0.071 | -           | 95(57.9) | 0.781     |             |    |            |

Data are mean±SD values or the percentage of individuals. Current/former smoker: the subject had ever smoked >10 cigarettes per day. Hypertension: blood pressure ≥140 mm Hg systolic or 90 mm Hg diastolic on repeated observations over 3 months, or if the subject was receiving chronic antihypertensive therapy. Dyslipidemia: total serum cholesterol level of >5.72 mmol/L (220 mg/dL).

*Statistical analysis was performed vs. controls. t-test or χ² were used to evaluate statistical differences between groups. Significance was accepted when p<0.05 (two-sided). †AG+GG genotypes, ‡CT+TT genotypes. ¶Multivariate analysis (hypertension, age, and sex included). ‡Multivariate analysis (diabetes mellitus, hypertension, and age included). DM: diabetes mellitus; ICH: intracerebral hemorrhage; IS: ischemic stroke; N/A: not available; SAH: subarachnoid hemorrhage.

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