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Association of polymorphisms of angiogenesis genes with breast cancer

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To the Editor

With great interest we have read the recent publication by Schneider et al. [1] about the association between polymorphisms of angiogenesis genes and breast cancer. The authors described an association of the VEGF-2578A and -1498C allele with increased breast cancer risk. These results are in contrast to our recent findings that VEGF polymorphisms are not associated with breast cancer risk [2]. Interestingly, Schneider and colleagues also investigated the influence of VEGF polymorphisms on metastatic disease progression and found no significant association.

Encouraged by that report, we have retrieved data on metastasis of the 839 breast cancer patients from our study and performed an analysis of the association between metastases and VEGF polymorphisms.

VEGF genotypes (-2578C>A, -2489C>T, 1498C>T, -634G>C, -7C>T, -936C>T, -1612G>A) were determined using 5'-nuclease assays (TaqMan). Reaction conditions were as described previously [2]. The study was performed according to the Austrian Gene Technology Act and has been approved by the local Ethical Committee. Written informed consent was obtained from all patients. According to breast cancer staging, patients were divided in three groups, representing patients without metastases ($n = 708$), those with metastases other than bone ($n = 69$), and those with bone metastases ($n = 62$). SPSS 14.0 for Windows was used for statistical analysis. Continuous values were analyzed by Student's t -test, and proportions of groups compared by the χ^2 test. Odds ratio (OR) and the 95% confidence interval (CI) were calculated to estimate the risk of bone metastasis. The level of significance was set at $P < 0.05$.

The frequency of the VEGF 1498 CC genotype was significantly lower among patients with bone metastases (6.5%) than among patients with metastases other than bone (23.2%; $P = 0.005$) or patients without metastases (23.4%; $P = 0.002$, Table 1). Odds ratio of the CC genotype for bone metastases was 0.22 (95% CI 0.08–0.61; $P = 0.004$). Genotype distribution of the other investigated VEGF polymorphisms did not show a significant association with metastases.

VEGF plays a critical role in tumor progression and distant tumor spread [3]. The present results suggest that the homozygous VEGF 1498 CC genotype might decrease the risk of bone metastases in breast cancer patients. However, further large prospective population based studies will be necessary before firm conclusions on the role of genetic risk factors for breast cancer metastases can be drawn.

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Table 1 VEGF -1498 T>C genotypes in breast cancer patients stratified by type of metastasis

	Group 1: No metastases	Group 2: metastases other than bone	Group 3: bone metastases
<i>n</i>	708	69	62
VEGF -1498			
TT	199 (28.1)	18 (26.1)	18 (29.0)
TC	343 (48.4)	35 (50.7)	40 (64.5)
CC	166 (23.4)	16 (23.2)	4 (6.5)

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