Letter to Editor

Emerging etiopathogenic connections between Arg399Gln polymorphism and systemic malignancies besides their etiological role in endometrial carcinomas

S. Kapoor

Private practise, Mechanicsville, VA (USA)

I read with great interest the recent article by Samulak *et al*. in a recent issue of your esteemed Journal [1]. The article is thought to be highly provocative. Interestingly, over the past few years, Arg399Gln polymorphism has been demonstrated to have a significant etiologic role in the development of other systemic malignancies besides endometrial carcinomas.

A close relationship exists between the Arg399Gln polymorphism and certain gynecological cancers. For example, an increased incidence of cervical cancer has been noted in females with the Arg399Gln polymorphism [2]. Female patients with the Gln/Gln genotype are 1.7 times more likely to develop cervical cancer in comparison to those exhibiting the Arg/Arg genotype. In addition, the presence of the Arg399Gln polymorphism predisposes African and Asian females to an increased risk of developing breast carcinomas [3].

Duman *et al*. have recently reported that certain chronic lymphoid leukemias may result because of Arg399Gln polymorphisms [4]. Similarly, the Gln399Gln genotype almost doubles the risk of developing childhood acute lymphoblastic leukemia especially in female populations [5]. In addition, the Arg399Gln polymorphism exhibits synergistic activity and increases the risk of developing childhood acute lymphoblastic leukemia by nearly 3.7 times when associated with the CYP2E1*5B polymorphism.

A similar etiopathogenetic role exists between gastric carcinomas and the Arg399Gln polymorphism [6]. Similarly, the Arg399Gln polymorphism significantly influences the prognosis in lung carcinoma patients [7]. Interestingly, in Asian populations, the presence of the Arg399Gln polymorphism confers an increased risk of developing prostatic malignancies [8]. The risk is increased almost by 43% in Asian men demonstrating the Gln/Gln genotype in comparison to those exhibiting the Arg/Arg genotype [9]. In fact, the Gln/Gln genotype exhibits synergism with smoking habits in increasing the incidence of prostate carcinoma [10]. A similar etiological connection has been established between bladder carcinomas and the Arg399Gln polymorphism [11].

The above examples clearly illustrate the etiologic role of Arg399Gln in the development of malignancies ranging from gastric carcinoma to chronic leukemia. Additional large-scale studies are needed to further identify the plausible role of the Arg399Gln polymorphism in the etiology of other systemic malignancies besides endometrial carcinomas.

References

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The editors in chief were not able to obtain a comment to the letter from Dr. Sumalek *et al*. which ever is appropriate.

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Address reprint requests to:
S. KAPOOR, M.D.
7487 Sherwood Crossing place # 302
Mechanicsville, VA 23111 (USA)
e-mail: shailendrakapoor@yahoo.com