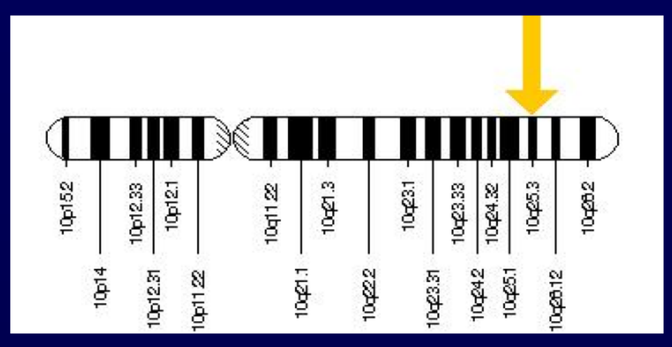
TCF7L2 gene variants predispose to development of type 2 diabetes among individuals with metabolic syndrome

Konstantinos Katsoulis[1], Stavroula A. Paschou[1], Elissavet Hatzi[2], Stelios Tigas[1], Ioannis Georgiou[1], Agathocles Tsatsoulis[1]

[1]Department of Endocrinology and Diabetes, Medical School, University of Ioannina, Greece
[2]Laboratory of Human Reproductive Genetics, University of Ioannina, Greece

Introduction: Transcription factor 7 like-2 (*TCF7L2*) gene variants (rs12255372 and rs7903146) have been consistently shown to raise genetic risk for type 2 diabetes (T2D). The aim of this study was to investigate the possible role of these variants in the development of impaired glucose metabolism (IGM), including impaired fasting glucose (IFG) or T2D, in patients with metabolic syndrome (MS).



Patients & Methods: We studied 228 patients with MS who were divided in two groups. The first group consisted of 148 patients with MS and IGM (39M/109F, 59.8±14.6 years) and the second group of 80 patients with MS without IGM (16M/64F, 56.1±15.8 years).
The diagnosis of MS was based on the criteria proposed by the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) Scientific Statement.
The BMI and the waist circumference were recorded and blood samples were obtained after overnight fasting for biochemical tests. The rs12255372 and rs7903146 *TCF7L2* polymorphisms were genotyped in peripheral blood leucocytes.

	Patients with IGM	Patients without IGM	*p* value
Number of patients	148/228 (64.9%)	80/228 (35.1%)	
Age(years)	59.8 ± 14.6	56.1 ± 15.8	0.075
Sex	39M (26.7%) 109F(73.3%)	16M (20%) 64F (80 %)	0.285
Weight (kg)	88.6 ± 17.3	87.3 ± 18.8	0.615
Height (cm)	160.9 ± 8.2	160.9 ± 8	0.990
BMI (kg/m^2)	34.2 ± 6	33.6 ± 6.4	0.507
Waist circumference (cm)	109.4 ± 12.2	107.7 ± 13.1	0.353
Hip circumference (cm)	109.9 ± 12.1	109.8 ± 14.6	0.952
W/H ratio	1 ± 0.1	0.99 ± 0.1	0.470
Hypertension	113/148 (76.4%)	60/80 (75%)	0.812
Dyslipidaemia	89/148(60.1%)	39/80 (48.8%)	0.098

Results:

♦ The frequency of the T allele of the *TCF7L2* variant rs12255372 was 38.2% in the study population.

♦ The frequency of the T allele of the *TCF7L2* rs7903146 variant was 35.3%.

Number of patients with MS	228
TCF7L2 rs12255372	
GG	81 (35.5%)
GT	120 (52.6%)
TT	27 (11.8%)
T allele	174/456(38.2%)
TCF7L2rs7903146	
CC	84 (36.8%)
CT	127 (55.7%)
TT	17 (7.5%)
T allele	161/456(35.3%)

♦ The T allele of rs12255372 variant was more frequently present in patients with MS and IGM (48.3%) compared to patients with MS without IGM (19.4%) (OR: 3.89, 95% CI: 2.47-6.12, p<0.0001).

♦ The T allele of rs7903146 was more frequently present in patients with MS and IGM (44.6%) compared to patients with MS without IGM (18.1%) (OR: 3.64, 95% CI: 2.29-5.78, p<0.0001).

Genotype	Patients with IGM	Patients without IGM	OR (95% CI)	p value
rs12255372				
GG	30/148 (20.3%)	51/80 (63.8%)	0.14 (0.08-0.27)	**<0.0001**
GT	93/148 (62.8%)	27/80 (33.8%)	3.32 (1.88-5.88)	**<0.0001**
TT	25/148 (16.9%)	2/80 (2.5%)	7.93 (1.83-34.41)	**0.001**
T allele	143/296 (48.3%)	31/160 (19.4%)	3.89 (2.47-6.12)	**<0.0001**
rs7903146				
CC	30/148 (20.3%)	54/80 (67.5%)	0.12 (0.07-0.23)	**<0.0001**
CT	104/148 (70.2%)	23/80 (28.7%)	5.86 (3.22-10.66)	**<0.0001**
TT	14/148 (9.5%)	3/80 (3.8%)	2.68 (0.75-9.63)	0.117
T αllele	132/296 (44.6%)	29/160 (18.1%)	3.64 (2.29-5.78)	**<0.0001**

Conclusion: The presence of variants rs12255372 and rs7903146 of the *TCF7L2* gene is associated with impaired glucose metabolism in patients with MS.

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Stavroula Paschou
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