Analysis of BclI, N363S and ER22/23EK polymorphism of the glucocorticoid receptor gene in a large series of patients with adrenal incidentaloma.

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GLUCOCORTICOID RECEPTOR AND POLYMORPHIC SITES

Some variants of the glucocorticoid receptor (GR) gene have been found to alter glucocorticoid sensitivity and have been associated with worsen metabolic profiles.

***ER22/23EK**
RESISTANCE

CORTISOL

***BCL I - *N363S**
SENSIBILITY

AIM OF THE STUDY

1. To asses whether the **prevalence** of 363S,ER22/23EK and BclI variants are d**ifferent** in patients with adrenal incidentaloma and/or subclinical Cushing syndrome than control subjects
2. To study whether the presence of these gene variants may be **linked to** metabolic or hormonal abnormalities in patients with adrenal incidentalomas or subclincal cushing syndrome

METHODS

411 subjects with adrenal incidentaloma

186 population-matched control subjects

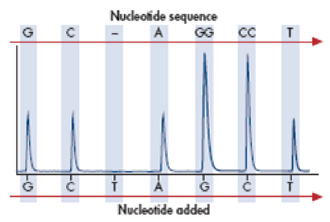
GENOTYPE

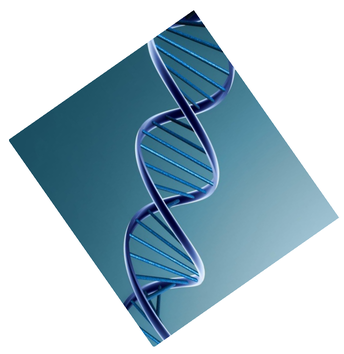
ER22/23EK
BCL I
N363S

PHENOTYPE

hypertension?
hyperglicemia?
dyslipidemia?
obesity?

DNA extraction
PCR
PYROSIQUENCING



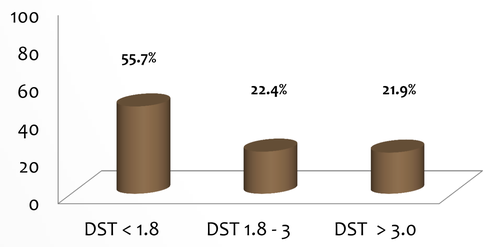


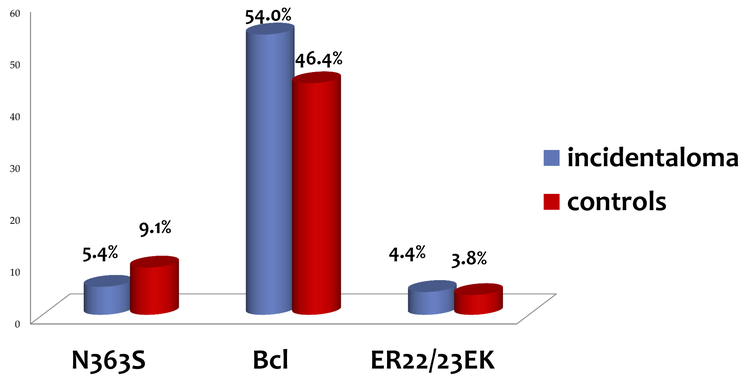
Patients were stratified by using Cortisol after 1 mg DST
- < 1.8 mcg/dl
- 1.8-3 mcg/dl
- > 3 mcg/dl

BMI (obesity >25Kg/m2)
WAIST (>102 cm men, >88 cm women)
BLOOD PRESSURE (>140/90 mmHg, or treatment)
HYPERGLICEMIA (glycemia >110 mg/dl or treatment)
DYSLIPIDEMIA (LDL cholesterol >160 mg/dl, HDL cholesterol <40 md/dl, triglycerides>150 mg/dl)

RESULTS

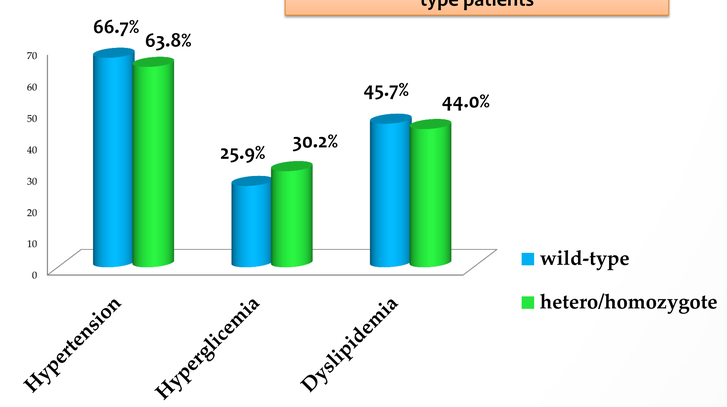
FREQUENCY OF POLYMORPHISMS





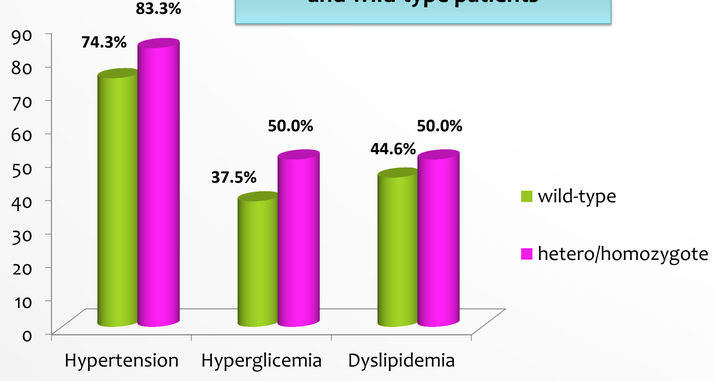
BCL I

No differences between carriers and wild-type patients



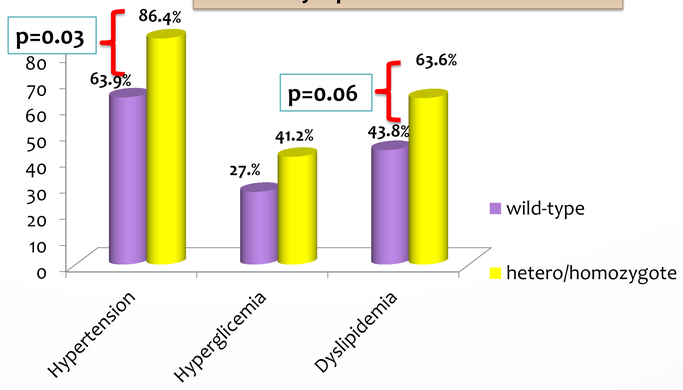
ER22/23EK

No differences between carrier and wild-type patients



N363S

Higher frequency of hypertension and dyslipidemia in carriers



MULTIPLE REGRESSION ANALYSIS
- R2 : 0.06
- p< 0.01

	AGE	SEX	BMI	N363S
HYPERTENSION (all patients)	p=0.06	p=0.02	p<0.01	**p=0.06**
HYPERTENSION (DST <1.8 mcg/dl)	p=0.05	p=0.02	p<0.01	**p= 0.015**

In patients with DST <1.8 µg/dl N363S variant seems to be an independent predictor of HYPERTENSION

We have not found any difference in the prevalence of the evaluated SNPs between patients and controls.

The GR variants are not associated with the development of adrenal incidentalomas

The ER22/23EK and BclI variants don't seem to have any influence on hormonal secretion and clinical presentation.

N363S could influence blood pressure levels. However, the effect seems to be more evident in patients with normal cortisol secretion, while it is less apparent in subjects with an autonomous cortisol secretion.

Cortisol secretion outweighs the effect of GC receptor sensitivity on clinical phenothype ?