

# PLASMA HUMANIN LEVELS DURING NORMAL CHILDHOOD AND PUBERTY. STUDY OF POSSIBLE CORRELATIONS WITH SEX, AGE, AND INSULIN LEVELS.



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## INTRODUCTION

Humanin is a novel signaling peptide which has been shown, by in vitro and in vivo studies, to improve insulin sensitivity. As plasma humanin levels decrease during adulthood, particularly during aging, it has been proposed that the increment of insulin resistance in aging might be associated with lesser humanin plasma values. We have hypothesized that the physiological insulin resistance observed during puberty development in normal children might be related to a physiological decrement of plasma humanin levels, however, there are no data of humanin levels available in normal children and adolescent of both sexes.

## AIM

To evaluate the developmental changes of plasma humanin levels in normal children of both sexes as a function of chronological age (CA), pubertal stage and insulin levels.

## STATISTICAL ANALYSIS

All statistical analyses were performed using Statistix 7 (Analytical software, Tallahassee, FL) Groups were compared using the Two-Sample T Test for normal data. Simple linear regression analysis between different pairs of variables was performed. In addition, Pearson's correlation test was used in order to compute the relationship between several variables studied and evaluate those linearly most associated with the dependent variable. An analysis of variance (one-way analysis variance) was used to test the differences between the groups and multiple comparisons (Bonferroni method) for normal data or data logarithmically transformed to obtain an approximately normal distribution

## MATERIALS AND METHODS

Blood samples from 163 subjects (69 girls and 94 boys) were studied. They were obtained at routine pre-surgery evaluations in subjects without endocrine or metabolic disorders. Inclusion criteria were that height, weight and BMI had to be within -2 and 2 SDSs.

## MATERIALS AND METHODS

- Serum levels of HN were measured using an in-house ELISA in USC Davis School of Gerontology, USA .
- Height was measured using Harpenden stadiometer, BMI was calculated.
- Height and weight were calculated based on Argentinean reference data. BMI SDS was calculated based on CDC reference data in > 5 yr old and WHO reference data in < 5 yr old.
- Pubertal stage was calculated according to Marshall and Tanner's criteria.

The females (F) were divided according to Tanner stage for breast (I-V) and the males (M) according to testicular volume(TV)

Gr 1F included 33 prepubertal girls.

Gr 2F included 36 pubertal girls: Gr 2aF Tanner II-III (early puberty; n= 12) and Gr 2bF Tanner IV-V (late puberty; n =24)

Gr 1M included 69 prepubertal boys

Gr 2M included 25 pubertal boys: Gr 2aM (early puberty;TV≤10cc; n=7) and Gr 2bM (late puberty; TV 12-25 cc; n=18)

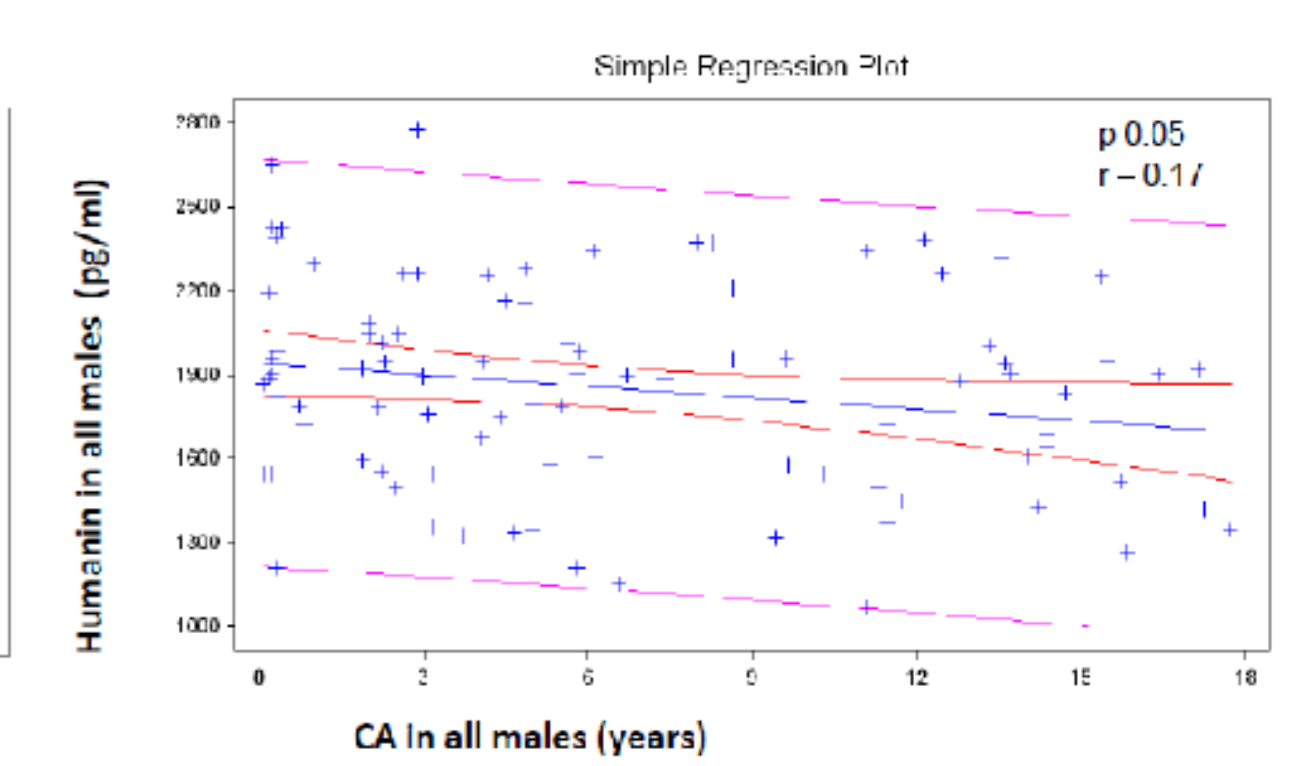
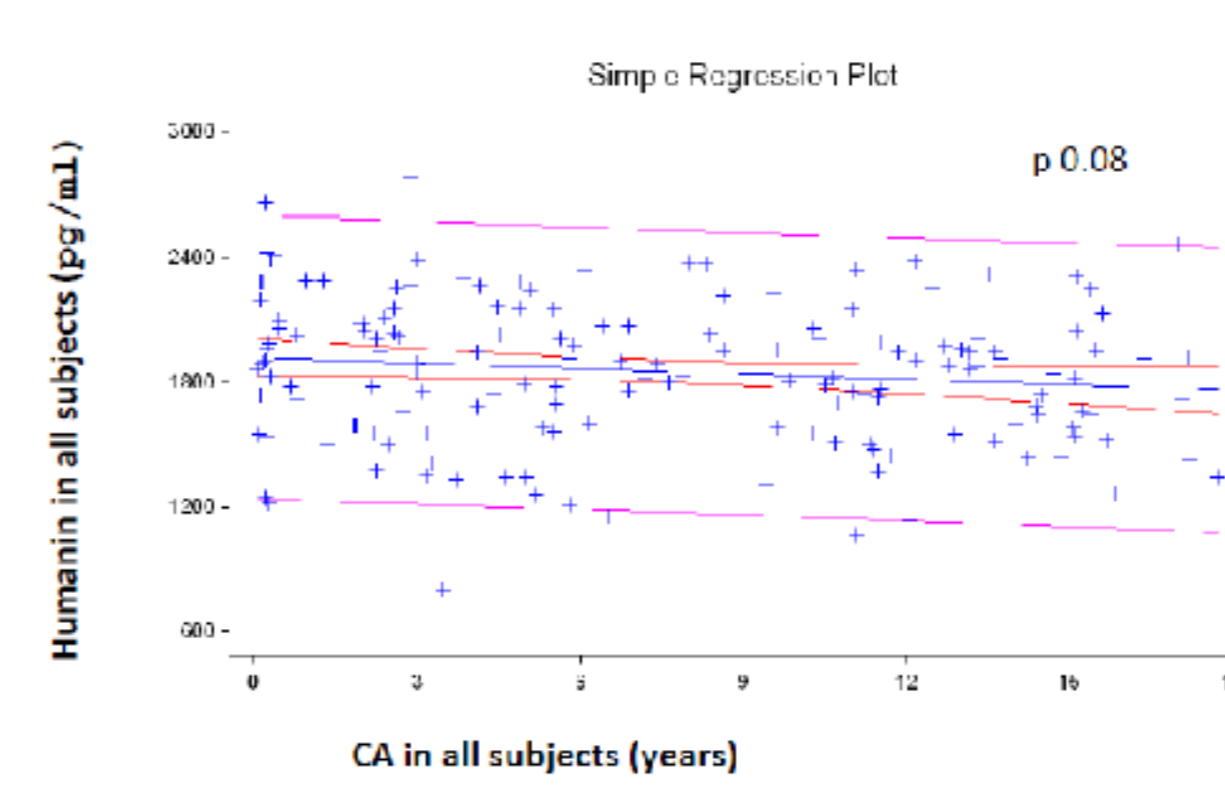
## RESULTS

### Analysis of humanin, CA and insulin in girls and boys Comparison of the different groups

F (n)	Humanin (pg/ml) X ± SD	CA (y) X (range)	Insulin (uUI/ml) X ± SD	M (n)	Humanin (pg/ml) X ± SD	CA (y) X (range)	Insulin (uUI/ml) X ± SD	M vs F p (T test) humanin	M vs F p (T test) insulin
All F (69)	1856.7 ± 314.55	8.84 (0.16-17.08)	6.5 ± 4.15	All M (94)	1852.7 ± 367.66	6.5 (0.08-17.72)	4.88 ± 3.60	0.94	0.008
Gr 1F (33)	1885.7 ± 350.55	4.23 (0.16-11)	3.20 ± 1.58	Gr 1M (69)	1892.8 ± 367.85	3.77 (0.08-11.08)	3.40 ± 2.04	0.93	0.61
Gr 2F (36)	1830.1 ± 279.92	13.08 (9.56-17.08)	9.5 ± 3.39	Gr 2M (25)	1742.1 ± 350.77	14.06 (11.08-17.72)	8.97 ± 3.82	0.28	0.55
Gr 2aF (12)	1846.5 ± 183.85	10.99 (9.56-12.16)	9.29 ± 3.09	Gr 2aM (7)	1761.9 ± 395.63	12.51 (11.08-13.72)	9.80 ± 3.48	0.60	0.74
Gr 2bF (24)	1821.8 ± 320.72	14.12 (10.32-17.08)	9.65 ± 3.59	Gr 2bM (18)	1734.4 ± 343.86	14.66 (11.48-17.72)	8.65 ± 4	0.40	0.39

### Linear regression analysis CA and humanin levels

Linear regression analysis CA - Humanin	
All	p = 0.08
F	p = 0.74
Gr 1F	p = 0.71
Gr 2F	p = 0.58
M	p = 0.05 r = -0.17
Gr 1M	p = 0.37
Gr 2M	p = 0.94

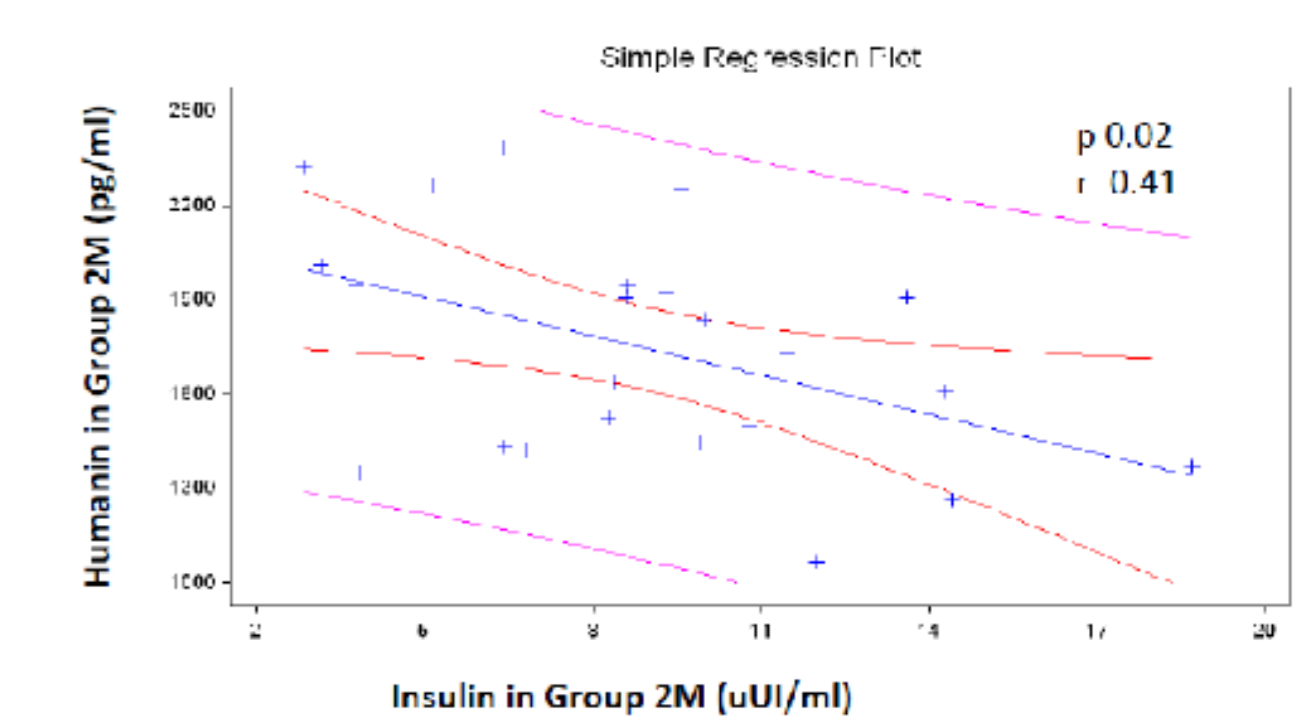
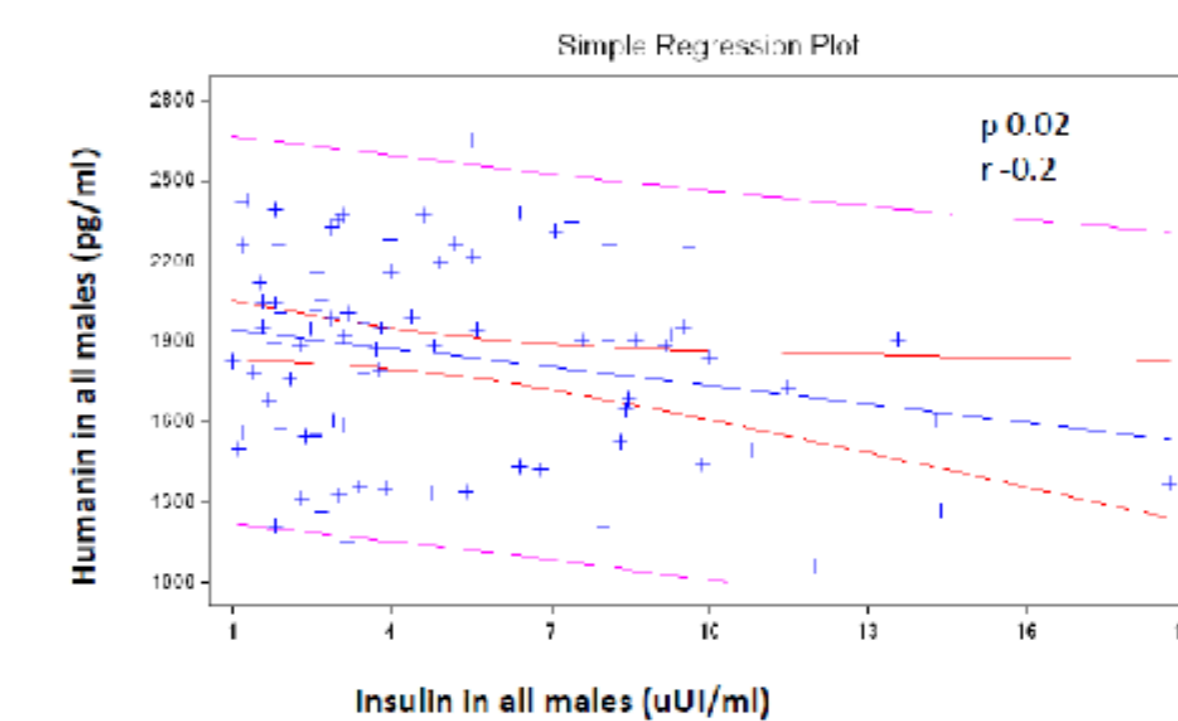


### Analysis of humanin, CA and insulin in all subjects

All subjects (n)	Humanin (pg/ml) X ± SD	CA (y) X (range)	Insulin (uUI/ml) X ± SD
163	1854.4 ± 345.1	7.49 (0.08-17.72)	5.57 ± 3.9

### Insulin and humanin levels

Linear regression analysis Humanin - insulin	
All	p = 0.02 r = -0.14
F	p = 0.35
Gr 1F	p = 0.39
Gr 2F	p = 0.22
M	p = 0.029 r = -0.2
Gr 1M	p = 0.72
Gr 2M	p = 0.023 r = -0.41



## CONCLUSIONS

- In all subjects plasma humanin levels do not change with CA
- No significant differences were found within humanin means in girls and boys of the different groups
- In boys the linear correlations analysis between plasma humanin levels and CA showed a tendency to decrease (p=0.05)
- A sexual dimorphism was observed in insulin/humanin correlation during puberty
- As non dynamic changes of plasma humanin levels in normal pre-pubertal and pubertal children of both sexes was observed, it seems that humanin might not be involved directly in the mechanism of physiological insulin resistance described in puberty. However, the relevancy of the sexual dimorphism in insulin/humanin negative correlation during puberty should be elucidated.

## REFERENCES

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