Congenital IGF-I Deficiency Protects from Cancer *Update 2010*

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The authors declare no conflict of interests

BACKGROUND

- **The link between IGF-I and malignancy is an accepted fact.**

- **Most cancerous tissues have an increased number of IGF-I receptors (1-2).**

1. Polak M, Nature Reviews cancer vol. 8 2008, 915-928
2. Donovan EA, Kummar S, *Crit Rev Oncol Hematol*. 2008; 66(2): 91–98.

BACKGROUND – ctd.

- **It has also been found that GH/IGF-I hypersecreting patients such as acromegalic or hGH transgenic animals are at a high risk for cancer development (3-4).**
- **Human population studies have demonstrated that high levels of circulating IGF-I are associated with an increased risk of certain malignancies (5).**

3. Holdaway I.M., Horm Res 2007; 68 (suppl 5):166–172
4. Tornell J. et al. , *Journal of Steroid Biochemistry and Molecular Biology 1992;* 43: 237–242
3. Haddad & Yee 2006, Fut Oncol 2: 101-110

BACKGROUND – ctd.

- **In a previous study (6) we have found that homozygous isolated congenital IGF-I deficiency (such as in Laron Syndrome, LS) protects patients from future development of malignancies.**
- **This was confirmed for the Ecuadorian cohort of LS patients (7).**

6. Shevah O, Laron Z. *GH & IGF Res 2007;17:51-57*
7. Guevara-Aguirre et al. *Horm Res 2007;68 Sup. 1:175*

AIM of STUDY

A. **To enlarge the number of patients with isolated congenital IGF-I deficiencies (LS, hGH-1 gene deletion, IGF-I gene deletion, IGF-I-R mutations, GHRH-R defects and congenital MPHD including hGH).**

B. **To find out whether congenital IGF-I deficiency combined with other pituitary hormone deficiencies also confers protection from cancer.**

SUBJECTS & METHODS

- **A total of 511 patients and 724 of their first-degree family members have been surveyed. The data was collected using a pre-structured questionnaire completed by endocrinologists in Israel and other countries; from the literature.**

- **The data includes our own cohort of 66 patients with Laron Syndrome, 25 with cong. IGHD and 25 cong. MPHD patients.**

SUBJECTS & METHODS

- 1/3 of the children with Laron Syndrome had long-term treatment with IGF-I, so did 5 adults patients for 9 months.
- ¾ of the cong. IGHD patients are known to be treated with hGH.
- Most of the cong. MPHD patients were treated with GH.

The above numbers were documented from our medical records, the questionnaire and from the literature.

RESULTS
Prevalence of malignancies

	Patients			First-degree Family members		
Diagnosis	**n**	**Age range (y)**	**Malignancies**	**n**	**Age range (y)**	**Malignancies**
Laron syndrome	217	1.5-75	0	201	1 - 81	18
Cong. IGHD	113	1.5-53	0	202	1 - 81	6
IGF-I R mutation	2	2.5 & 30	0	not surveyed	-	-
IGF-I gene deletion	2	6.5 &11.5	0	2	40 & 45	0
GHRH-R defects [8]	75	2.8-88	1M Hodgkin's lymph., 2M skin cancer	139	3 - 93	0
Cong. MPHD	102	0.25-86	1F thyroid Ca. diagnosed at 10.5y	180	1 - 84	4 + 1 susp.

RESULTS
Type of cancer

	First degree relatives			patients	
Cancer type	LS	Cong. IGHD	Cong. MPHD	GHRH-R defects	Cong. MPHD
Colon	-	2	-	-	-
Breast	3	2	-	-	-
Genitourinary tract	8	-	-	-	-
Gastric	2	-	1	-	-
Lung	1	-	-	-	-
Thyroid	1	-	-	-	1
Esophagus	1	-	-	-	-
Liver	1	-	-	-	-
Skin	1	-	-	2	-
Bone	-	1	1	-	-
Hemato.	-	1	-	1	-
Unknown	-	-	2 + 1 susp.	-	-

RESULTS

Two findings are evident:

1. **Patients with congenital isolated hGH or IGF-I deficiency are protected from cancer, whereas heterozygous (first degree relatives) are not.**

2. **Few patients with GHRH-R defects and cong. MPHD developed cancer.**

CONCLUSIONS

- **The present study underlines the important role cong. IGF-I deficiency has on the development of malignancies.**
- **Despite long term replacement treatment with IGF-I or hGH, no patient with LS or cong. IGHD reported cancer.**

CONCLUSIONS – ctd.

- **Not all patients with GHRH-R or cong. MPHD are protected from cancer. The explanation for the development of cancer is that some patients secrete small amounts of hGH** (8).
- **Our findings justify the use of antibodies against IGF-I or it's receptor in the treatment of malignancies.**

8. Aguiar-Oliveira et al. *JCEM 2010*;95:714-721

Acknowledgments

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Thank you for your
ATTENTION