

Increased serum concentrations of HSP 90 in patients with thymic epithelial tumors

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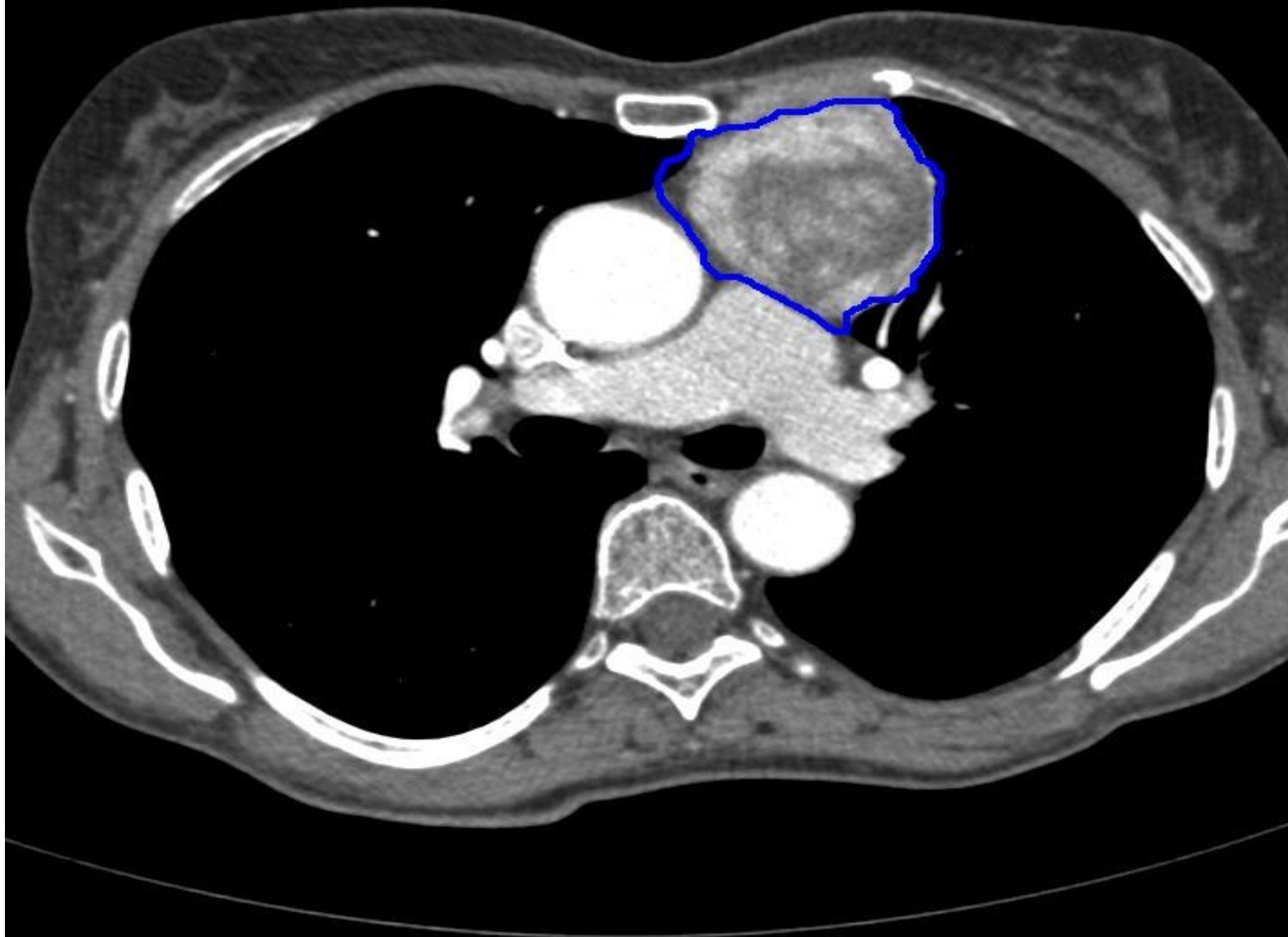
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Department of Thoracic Surgery*

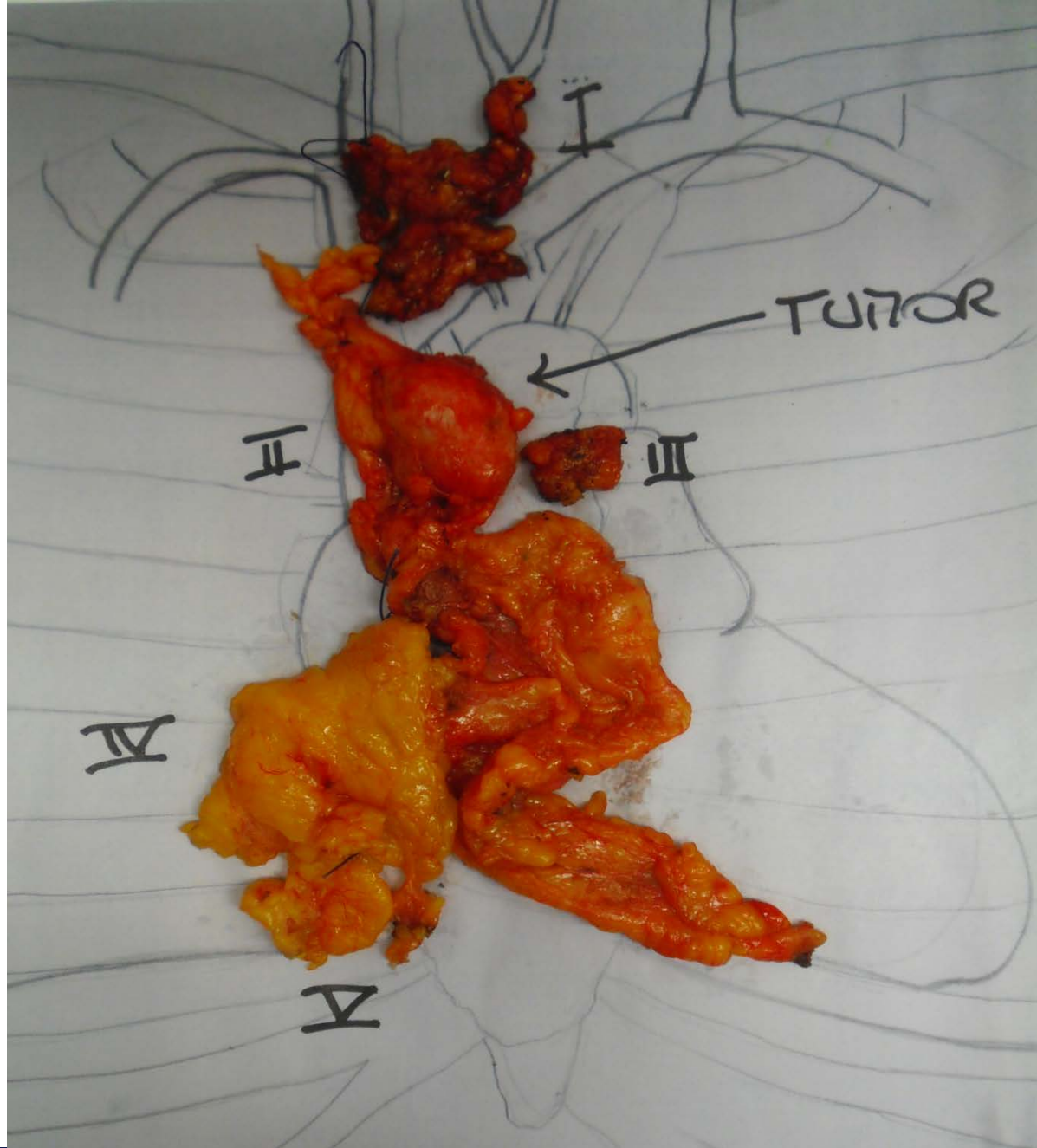




Disclosure slide

We have no financial relationships
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Orphan disease:

Thymic Epithelial Tumors (TETs)

TET Incidence: *0.2-1.5%* of all malignancies¹
2-4 per 1,000,000

BUT: *most common anterior mediastinal tumor in adults*

Myasthenia Gravis (MG)

- **10-15%** of MG patients have TETs
- **30-50%** of patients with TETs have MG

¹Engel P, Marx A, Muller-Hermelink HK. Thymic Tumours in Denmark. A retrospective study of 213 cases from 1970-1993. Pathol Res Pract (1999); 195: 565 - 570

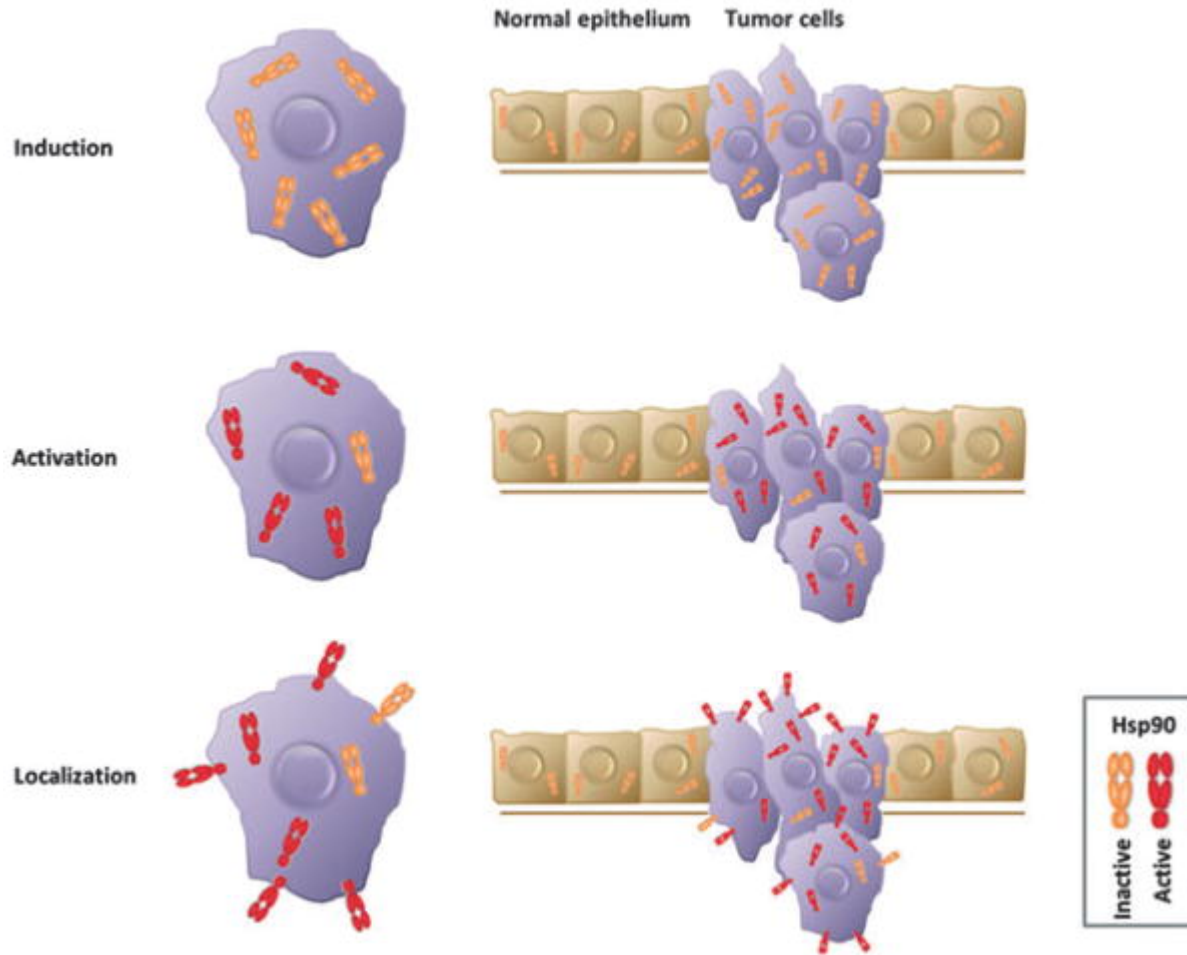


Background – heat shock proteins (HSPs)

- **Induced by different kind of stressors** (heat, oxidative stress, hypoxia,...)
- **Classified according to molecular weight**
HSP100, HSP90, HSP70, HSP60, HSP40 and small HSPs (HSP27) ¹
- **Main functions**
 1. Molecular chaperones: protein (re-)folding, transport, homeostasis
 2. Inhibition of apoptosis: extrinsic and intrinsic pathway
- **HSPs in cancer** -> associated with tumor growth, resistance to chemotherapy, metastases and poor clinical outcome ¹

¹ Khalil AA. et al. Heat shock proteins in oncology: diagnostic biomarkers or therapeutic targets? Biochem Biophys Acta (2011);1816:89-104

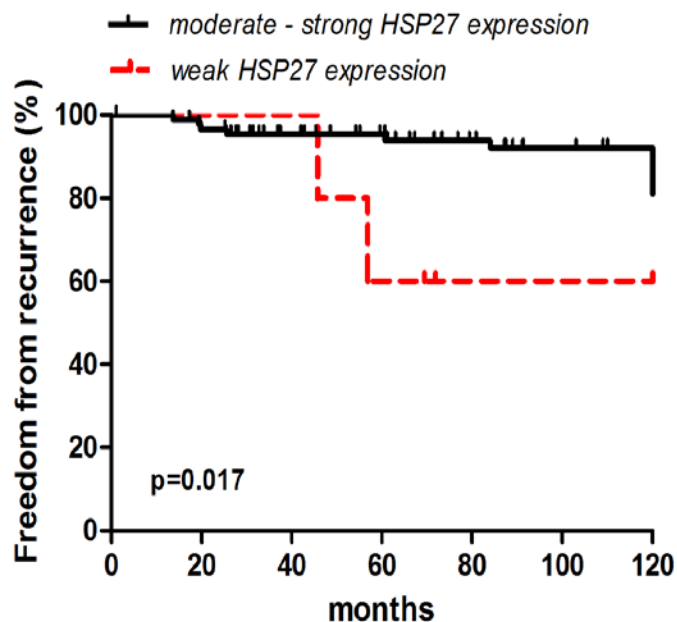
Heat shock protein 90 - Secretion



Barrott JJ, Haystead TA. Hsp90, an unlikely ally in the war on cancer. FEBS J. 2013 Mar;280(6):1381-96. doi: 10.1111/febs.12147. Epub 2013 Feb 24.

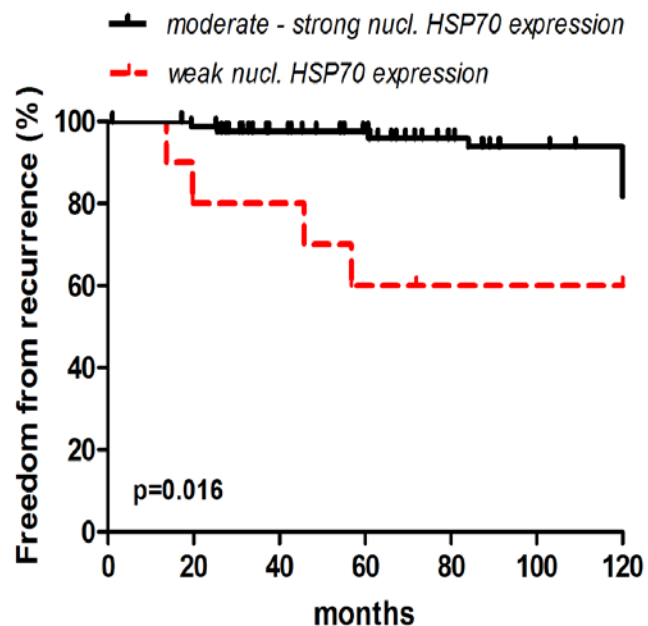
Freedom from recurrence

Cytoplasmic HSP27



<i>mod / str</i>	90	83	70	63	53	45	41
<i>weak</i>	5	4	4	3	1	1	1
	Numbers at risk						

Nuclear HSP70



<i>mod / str</i>	85	80	67	60	49	41	37
<i>weak</i>	10	8	8	6	5	5	5
	Numbers at risk						

Janik S, Schiefer AI, Bekos C, Hacker P, Haider T, Moser J et al. HSP27 and 70 expression in thymic epithelial tumors and benign thymic alterations: diagnostic, prognostic and physiologic implications. *Sci Rep* 2016; 6:24267. doi: 10.1038/srep24267.



Methods - HSP90alpha

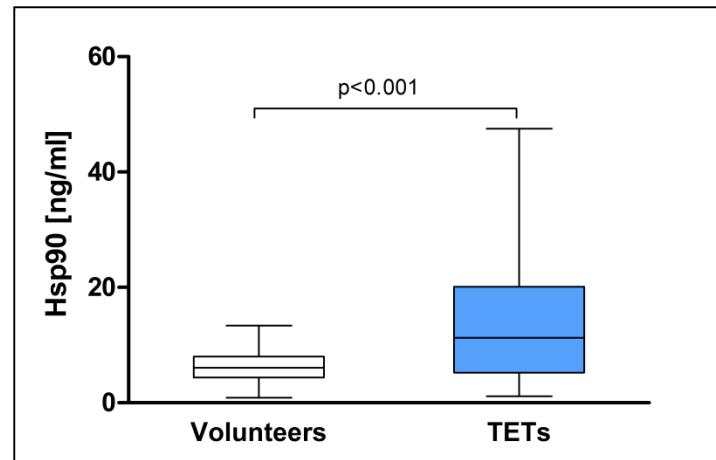
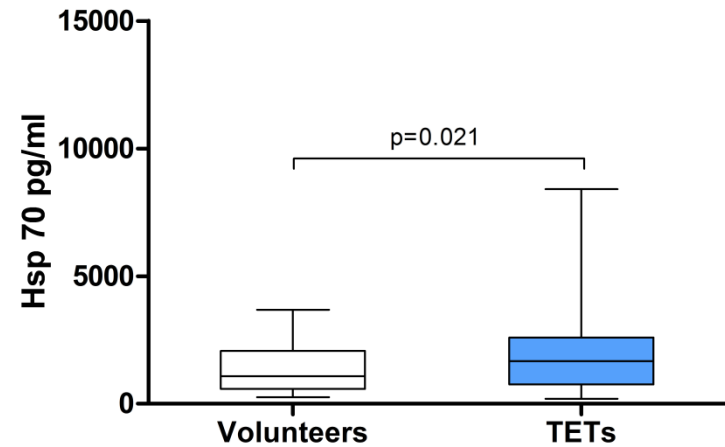
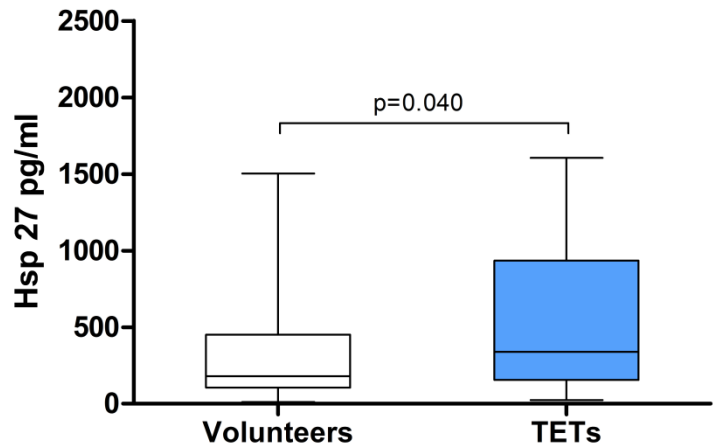
Division of Thoracic Surgery, Medical University of Vienna, Austria.

Study Population

- **58** healthy volunteers
- **114** patients with TETs: **86** thymomas and **28** Thymic Carcinomas
- **20** patients with benign thymic pathologies

ELISA tests for **HSP90alpha**

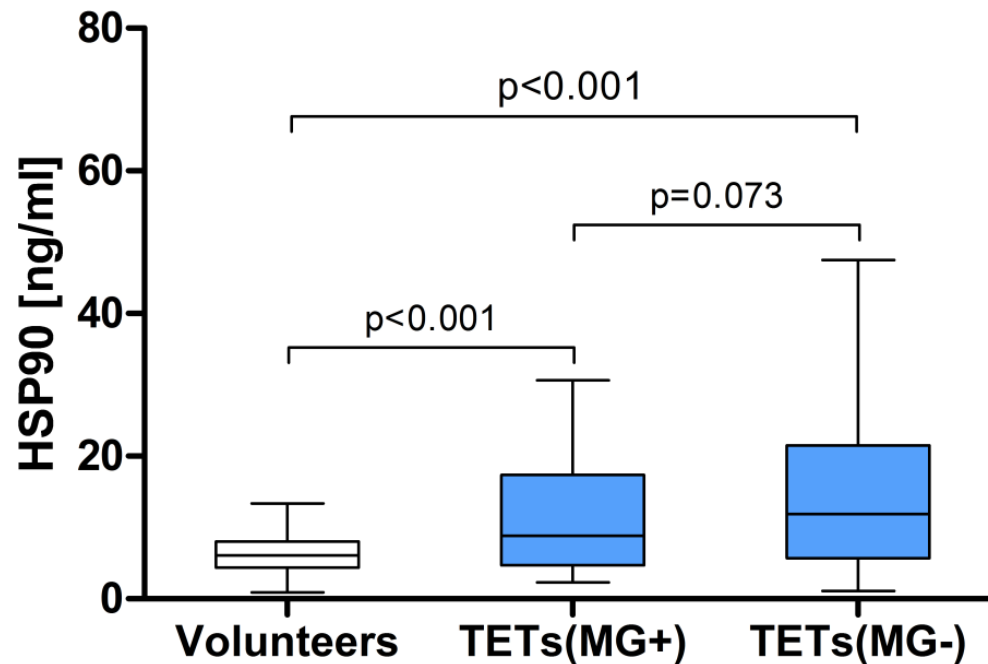
HSP serum concentrations in patients with TETs



Adapted from: Janik S, Schiefer AI, Bekos C, Hacker P, Haider T, Moser J et al. HSP27 and 70 expression in thymic epithelial tumors and benign thymic alterations: diagnostic, prognostic and physiologic implications. *Sci Rep* 2016; 6:24267. doi: 10.1038/srep24267.

Results (1)

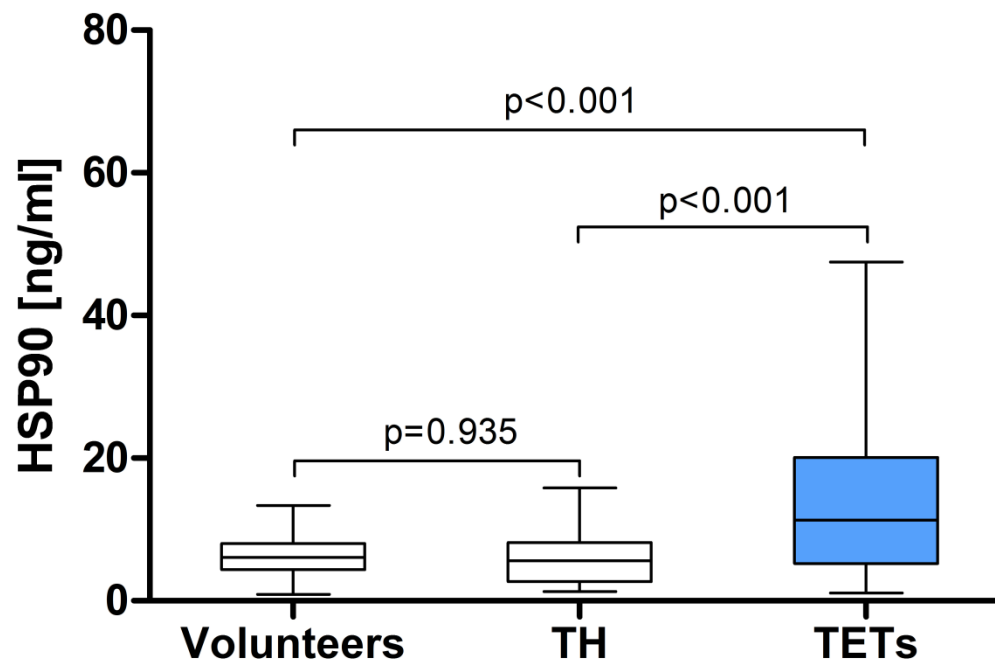
Serum concentrations of HSP90 in TETS +/- MG



TETs(MG+): n=31 TETs(MG-): n=83

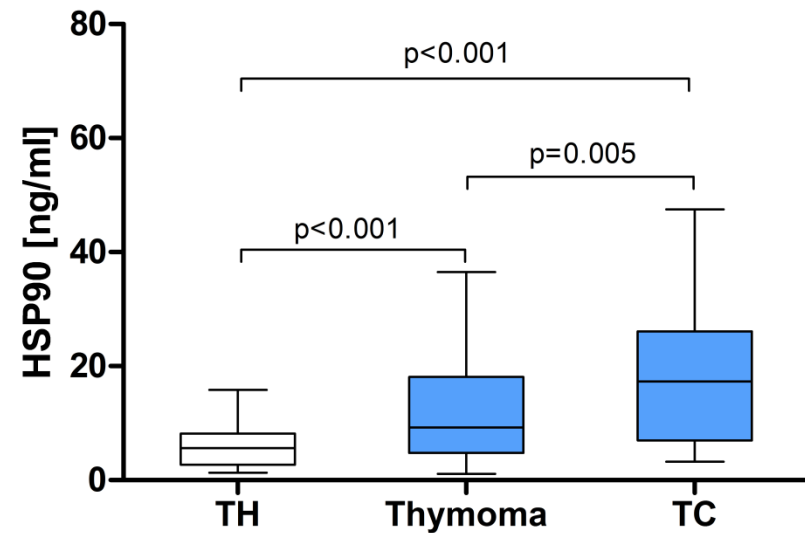
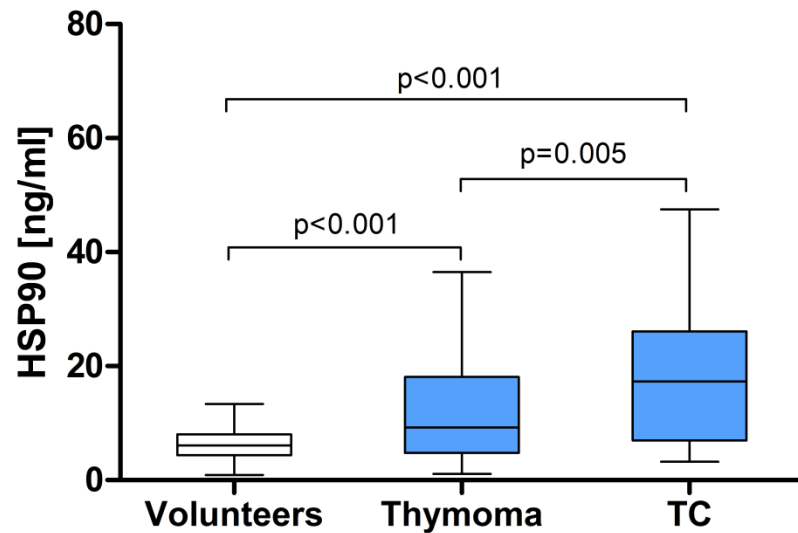
Results (2)

Serum concentrations of HSP90 in TETs vs. TH



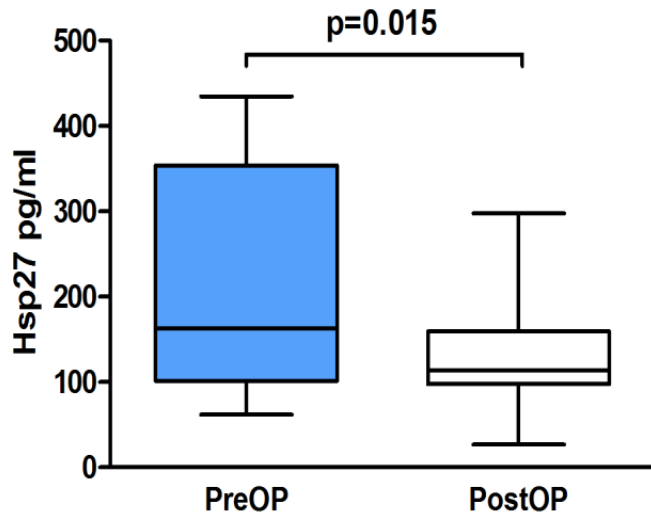
Results (3)

Serum concentrations of HSP90 TC vs. Thymomas vs. TH

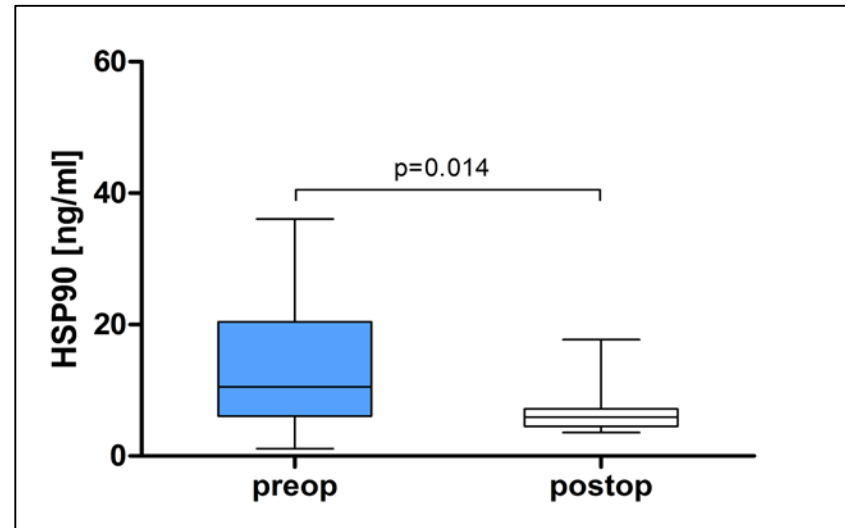


Results (4)

HSP serum concentrations after complete surgical tumor resection



n=16



n=13

Pre OP

- One day before surgery

Post OP

- at least one month after surgery
- No sign of recurrence



Summary

1. **HSP90** is highly secreted in TETs (*marker for diagnosis*)
2. **Strongest serum concentration** of HSP90 was found in TCs
(*tumor behaviour*)
3. **Tumor resection** → significant **decrease** of HSP90 serum concentrations
(*Follow up*)
4. **Elevated levels** of HSP90 in **myasthenia gravis** (*Pathogenesis*)

Conclusions

The analysis of heat shock proteins in patients with thymic epithelial tumors warrants further study.