BIOINFORMATICS APPROACH TO THE PETO PARADOX

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ABSTRACT

- The Peto paradox is a model that states that body size is not associated with lifespan between species in cancer occurrences.
- Tumor suppressor genes play an important role in cell cycle control, correction of DNA and chromosome errors, directing the cell to apoptosis in cases of irreparable damage, and prevention of metastasis.
- In our study, P53, MSH2, CADM1 and NOTCH1 proteins, which play a role in the regulation of various cellular events as tumor suppressors, were studied.
- At the end of the bioinformatics studies, it was determined that the *Homo sapiens* P53 protein similarity rate was low in *Ramazzottius varieornatus* and *Balaenoptera musculus* species. It was determined that MSH2, CADM1 and NOTCH1 proteins have high similarity rates between *Homo sapiens* species and *Balaenoptera acutorostrata scammoni* species.

Why are large animals less likely to get cancer?

The excess of Tumor Suppressor Genes reduces the likelihood of these creatures getting cancer.

INTRODUCTION

- Cancer (malignant neoplasia) is the uncontrolled cell proliferation observed in most multicellular organisms.
- Cancer-resistant animals can show evolutions that will prolong their life span, thanks to a decrease in the copy number of oncogenes, an increase in the copy number of tumor suppressor genes, a decrease in metabolic rate, a decrease in free radical production, an increase in immune resistance, and hypertumor formation (Caulin and Maley, 2011).
- Proteins such as p53 (Cellular tumor antigen p53), MSH2 (DNA mismatch repair protein Msh2), CADM1 (Cell adhesion molecule 1), NOTCH (Neurogenic locus notch homolog protein 1) and FAS (Tumor necrosis factor receptor superfamily member 6) act as tumor suppressors is in charge.
- 61 complete copy numbers of TP53 were characterized, including the African elephant (Loxodonta africana), Balaena mysticetus, Balaenoptera acutorostrata scammoni whales, and large long-lived mammals (Sulak et al, 2016).
- High-mass animals were shown to have more tumor suppressor genes (Sulak et al., 2016).
- In our study, we determined the similarities of the related proteins by detecting common tumor suppressor genes in humans with blast analyzes of creatures living in polar regions and resistant to cancer.

METHOD

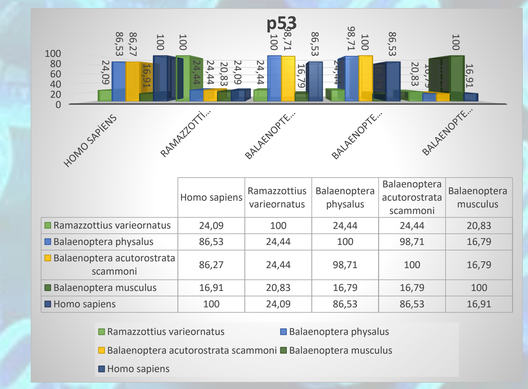
KEGG→ detection of common genes

UNİPROT – NCBI→ Detection of protein sequences

CLUSTAL OMEGA→ Similarity detection

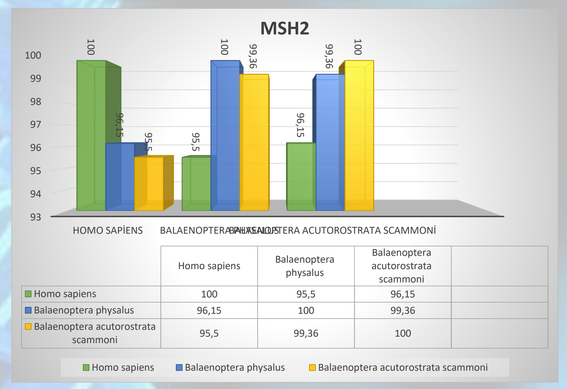
RESULTS

In our study, the sequence sequences of P53, MSH2, CADM1 and NOTCH1 proteins in selected organisms were determined by the Clustal omega program. Related proteins in homo sapiens were blasted using the NCBI database, respectively. In this way, possible sequence sequences and similarities of the related proteins in other living things were determined.



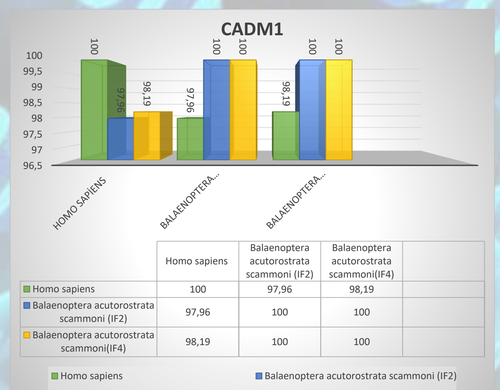
	Homo sapiens	Ramazzottius varieornatus	Balaenoptera physalus	Balaenoptera acutorostrata scammoni	Balaenoptera musculus
Ramazzottius varieornatus	24,09	100	24,44	24,44	20,83
Balaenoptera physalus	86,53	24,44	100	98,71	16,79
Balaenoptera acutorostrata scammoni	86,27	24,44	98,71	100	16,79
Balaenoptera musculus	16,91	20,83	16,79	16,79	100
Homo sapiens	100	24,09	86,53	86,53	16,91

Ramazzottius varieornatus · Balaenoptera physalus · Balaenoptera acutorostrata scammoni · Balaenoptera musculus · Homo sapiens



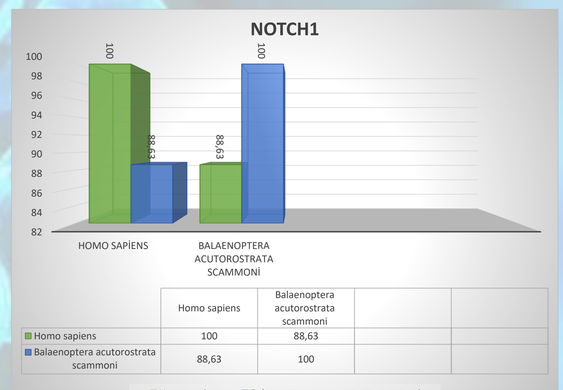
	Homo sapiens	Balaenoptera physalus	Balaenoptera acutorostrata scammoni
Homo sapiens	100	95,5	96,15
Balaenoptera physalus	96,15	100	99,36
Balaenoptera acutorostrata scammoni	95,5	99,36	100

Homo sapiens · Balaenoptera physalus · Balaenoptera acutorostrata scammoni



	Homo sapiens	Balaenoptera acutorostrata scammoni (IF2)	Balaenoptera acutorostrata scammoni(IF4)
Homo sapiens	100	97,96	98,19
Balaenoptera acutorostrata scammoni (IF2)	97,96	100	100
Balaenoptera acutorostrata scammoni(IF4)	98,19	100	100

Homo sapiens · Balaenoptera acutorostrata scammoni (IF2) · Balaenoptera acutorostrata scammoni(IF4)



	Homo sapiens	Balaenoptera acutorostrata scammoni
Homo sapiens	100	88,63
Balaenoptera acutorostrata scammoni	88,63	100

Homo sapiens · Balaenoptera acutorostrata scammoni

CONCLUSION AND DISCUSSION

- There are 3 arguments related to the resistance of large-bodied animals to cancer.In our studies, Homo sapiens P53 protein has 16.91% similarity *with Ramazzottius varieornatus* and 20.83% with *Balaenoptera musculus*. Considering the results, it was determined that there were high differences in common gene regions. *Homo sapiens* MSH2 protein was found to be 95.50% in *Balaenoptera physalus* and 96.15% in *Balaenoptera acutorostrata scammoni*. It was determined that homo sapiens CADM1 protein has a similarity rate of 97.96% with *Balaenoptera acutorostrata scammoni* (isoform X2) and 98.19% with *Balaenoptera acutorostrata scammoni* (isoform X4). It was determined that *Homo sapiens* NOTCH1 protein had a similarity rate of 88.63% *with Balaenoptera acutorostrata scammoni.* Considering the results, it was seen that MSH2, CADM1 and NOTCH1 proteins had a high similarity rate in the organisms we selected.
- *Homo sapiens* P53 mutagenez **bölgeleri 15. a. a S→A, 18 a. a T→A, 20 a. a S→A, 22-23 a. a, 24 a. a K→R, 37. a. a S→D, 46 a. a S→A, 55 a. a T→A, 183 a. a S→A, 248 a. a R→S, 269 a. a S→A, 284 a. a T→E, 291-292 a. a KK→RR, 319 a. a K→A, 320 a. a K→A, 321 a. a K→A, 333- 337 a. a RGRER→KGKEK, 359 a. a P→D, 361 a. a G→E, 362 a. a S→A, 370 a. a K→R, 372 a. a K→R, 373 a. a K→R, 382 a. a K→A, 383 a. a L→A, 385 a. a F→A, 386 a. a K→A, 387 a. a T→A, 388 E→A** and the possible effects of these mutations were determined in previous studies.(Shouse, Chai, Liu, 2008; Chehab, Malikzay, Stavridi, Halazonetis, 1999; Jung vd, 2011; Sun vd., 2007; Hofmann vd., 2002; Li, Li , Sheppard, Liu, 2004).
- *Homo sapiens* MSH2 protein mutagenesis region in the study, **675 a. a** determined to be a **K→R.** (Iaccarino, Marra, Palombo, Jiricny, 1998).
- In studies with *Homo sapiens* CADM1 protein, 2 mutagenesis sites **406 a. a Y→A** and **408 a. a T→A** (Busam, 2011).
- 2 mutagenesis shadows in studies with *Homo sapiens* NOTCH1 protein 1728 a. a P→C and 1755-1761 a. a deletion detected (Guanghui vd., 2019).

SUGGESTIONS

Our study can be supported by RT-PCR and cell culture studies on MSH2, CADM1 and NOTCH1 proteins in vitro.

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