

## PROVA ORALE 1

1. L'approccio NGS può essere utilizzato per patologie genetiche dovute a mutazioni somatiche?
2. Qual è l'organo deliberante del Dipartimento?
3. Quali tra quelle indicate sono unità di input?
  - a- Tastiera e monitor
  - b- Monitor e stampante
  - c- Tastiera e mouse

Somatic missense variants in TRAF7, concentrated within the WD40 domains and frequently recurrent, have been identified in meningiomas, mesotheliomas, intraneural perineuriomas and adenomatoid tumors of the genital tract. 10-17 Heterozygous germline variants in TRAF7 have recently been reported in seven patients with a developmental disorder involving cardiac, facial, and digital anomalies and developmental delay (OMIM#618164). Here, we refine our understanding of the TRAF7 mutational and phenotypic spectrum through the identification of 45 previously underscribed patients, and thereby define a syndrome with a recognizable facial gestalt, specific skeletal and cardiac defects, and developmental delay/intellectual disability, which we propose to name the TRAF7 syndrome

F. to La Commissione

## PROVA ORALE 2

1. Qual è l'utilità dell'approccio targeted – sequencing nell'analisi dei tumori?
2. Quali sono gli organi della Sapienza? un breve cenno a ciascuno di essi.
3. Il tasto escape (esc)
  - a- Serve a confermare le scelte e i comandi
  - b- Serve ad annullare l'operazione in corso
  - c- Serve a cancellare i caratteri alla sinistra del cursore

These effects are thought to be mediated by synergy between TRAF7 and the MAP3 kinase MEK3, leading to the phosphorylation of JNK and p38 ( regulators of AP1 and CHOP ), with interaction of TRAF7 and MEKK3 occurring via the TRAF7 WD40 repeats. 2,3 Depending on the context, TRAF7 can positively or negatively regulate the activity of NF- $\kappa$ B, through ubiquitination of pathway components p65 and NEMO.2,5,6 It also ubiquitinates p53, and the activity of the proto- oncogene c- Myb is negatively regulated by TRAF7 through sumoylation and consequent in the cytosol.

F. to La Commissione

### PROVA ORALE 3

1. Esempi di applicazioni dell'NGS per finalità di targeted Therapy
2. Quali sono le funzioni del Nucleo di Valutazione di Ateneo?
3. I tasti col simbolo delle frecce
  - a- Servono a cancellare i caratteri ai lati del cursore
  - b- Servono a spostare il cursore o la selezione di oggetti e menù
  - c- Servono ad attivare le applicazioni

Genotyping testing was performed according to approved ethical guidelines of the relevant institutions and consent was obtained from all families (including written consent to publish photographs, where applicable) Exome sequencing was performed in various independent research or diagnostic laboratories worldwide, using standard approaches (details available upon request). Targeted capture sequencing of TRAF7, in a panel of genes implicated in craniofacial malformations, was performed during clinical diagnostic screening at the Necker Hospital, using a SureSelect kit (Agilent) for capture followed by Castilla-Vallmanya et al. Polyphen-219 was used for predicting the pathogenicity of missense variants.

F. to La Commissione

#### PROVA ORALE 4

1. Qual è l'utilità della consulenza genetica pre e post test?
2. Quali sono gli organi del Dipartimento
3. Il tasto di reset
  - a- Serve a riavviare il computer azzerando programmi e dati memorizzati nella RAM
  - b- Serve a riavviare il computer azzerando programmi e dati memorizzati nell' hard disk
  - c- Serve a spegnere il computer

The WD40 repeats are unique to TRAF7 within the TRAF family, with all other members instead containing a C-terminal TRAF domain. In vitro studies have suggested that TRAF7 plays a role in the regulation of several transcription factors through various mechanisms. It participates in the signal transduction of cellular stress stimuli, such as TNF $\alpha$  stimulation, by activating pathways leading to increased transcriptional activity of AP1 and CHOP/gadd153. These effects are thought to be mediated by synergy between TRAF7 and the MAP3 kinase MEKK3, leading to the phosphorylation of JNK and p38 ( regulators of AP1 and CHOP), with interaction of TRAF7 and MEKK3 occurring via the TRAF7 WD40 repeats. Depending on the context, TRAF7 can positively or negatively regulate the activity of NF-Kb, through ubiquitination of pathway components p65 and NEMO.

F. to La Commissione

## PROVA ORALE 5

1. Che cosa sono i test genetici predittivi?
2. Chi conferisce l'incarico al Direttore Generale
3. Il modem
  - a- Serve a parcheggiare temporaneamente dati e programmi.
  - b- Costituisce l'unità centrale di elaborazione di dati e programmi.
  - c- Serve a mandare e ricevere dati connettendosi ad una rete telematica tramite una comune linea telefonica.

We performed exome sequencing, targeted capture sequencing and Sanger sequencing on individuals with undiagnosed, syndromic developmental delay/intellectual disability and dysmorphic facial features, in several independent clinical or research centers. Comparison of phenotypes and variants was facilitated by the data exchange platforms GeneMatcher<sup>20</sup> and DECIPHER.<sup>21</sup> We identified 45 individuals harboring missense variants in TRAF7 (Table S1 ).The cohort includes 36 sporadic cases in which the TRAF7 variant was the novo, one patient with low level maternal mosaicism from the TRAF7 variant, five cases with unknown inheritance and one familial case ( patients 24-26 ) in wich affected dizygotic twins inherited a TRAF7 variant from their affected mother, in whom the variant arose de novo (Figure S1).

F. to La Commissione