Post-translational modifications of histones linked with gliomas: H3K27me3

(*¿Methylated or Demethylated?, that is the question*)

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Introduction: key questions

➢ Why gliomas?

↪ Gliomas are **primary tumors with the highest onset rate in adulthood** and furthermore, they are **fatally aggressive**.

➢ Why PTM?

↪ Because of their remarkable role in **gene expression regulation** (activation and repression).

➢ Why this H3K27me3modification?

↪ H3 is the **most modified histone**.

↪ Lysine methylation is very complex: **multiple valences**.

↪ It is a **heterochromatic state** marker: transcriptional repression.

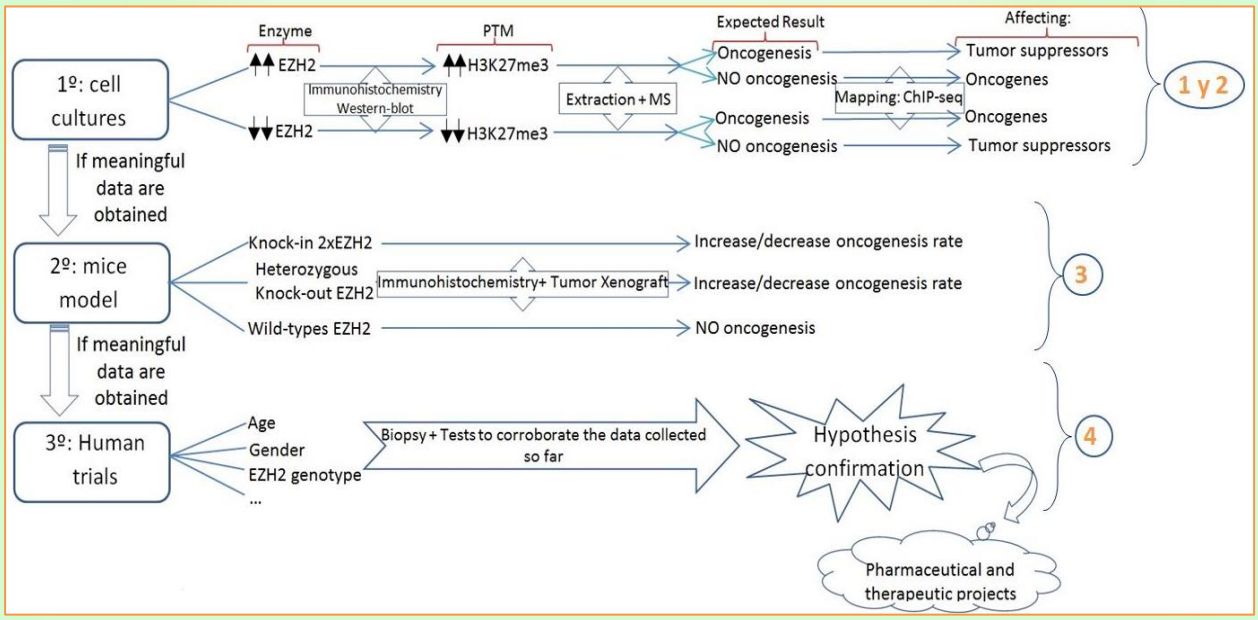
Goals

❖ Main goal: To prove the **role of post-translational modification H3K27me3** on gliomas onset and development.

❖ Collateral objectives:

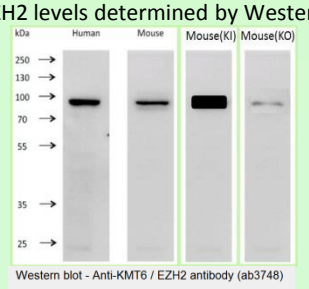
1. **Mapping which genes are affected** by the H3K27me3 modification in order to be able to link it with the associated phenotypes.
2. **Analyzing the effects** of overexpression or inhibition depending on which genes are affected by PTM.
3. **Studying the histological consequences** using a mice model.
4. **Corroborate the previous results**, now with human trials, so that a valid diagnosis tool or a good therapeutic target can be assessed.

Project outline



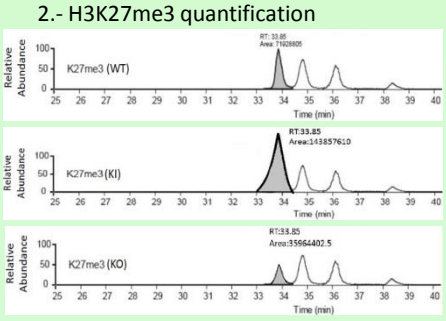
Expected results

1.- EZH2 levels determined by Western-blot:



All lanes : Anti-KMT6 / EZH2 antibody (ab3748) at 1/1000 dilution.
Lane 1 : HEK293 cell lysate; **Lane 2 :** Mouse hippocampus cell lysate
Secondary: HRP-conjugated Mouse anti-rabbit IgG at 1/5000 dilution developed using the ECL technique.

2.- H3K27me3 quantification



Mass Spectrometry expected profile. Image adapted from ninth bibliography reference: Forné, I., Barth, T., & Imhof, A. "Quantifying histone modifications using mass spectrometry (Prot 51), *Epigenesys*, 2012; 1–14.

3.- Immunohistochemistry assays with mice tissues