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Tet2 is required to resolve inflammation by recruiting Hdac2 to specifically repress IL-6

Qian Zhang, Kai Zhao et al

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DNA methylation

- Is a process of epigentics that stops DNA transcription by adding a methyl-group (CH_3) to the major groove of DNA

- Most common methylation is a covalent binding at the 5-carbon of the cytosine ring
- Product: 5-methylcytosine (5-mC)

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DNA methylation

- DNA methyltransferases (DNMTs) catalyze and/or stabilize the addition of the methylgroup from s-adenosylmethionine
- Ten eleven translocation (TET-family) of 5-mC hydoxylases proceeds active demethylation
- TETs (and DTNM) hydroxylate 5-mC resulting in 5-hmC (important e.g. for tumor suppression)

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DNA methylation

- 5-hmC plays a role in gene transcription and demethylation

- TET1: transcriptional activation and repression
- TET2: tumor suppression
- TET3: reprogram DNA methylation

- DNA demethylation intermediate product is 5-fC

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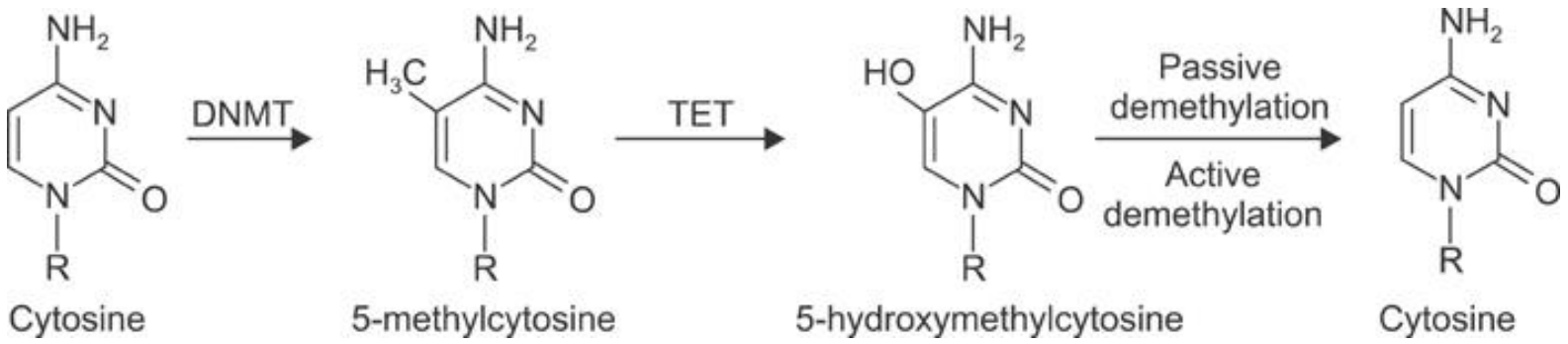
DNA methylation



Ji Woong Son, M.D., Ph.D, Year-in-Review of Lung Cancer. Tuberc Respir Dis. 2012 Sep;73(3):137-142. English.
Published online September 28, 2012. http://dx.doi.org/10.4046/trd.2012.73.3.137

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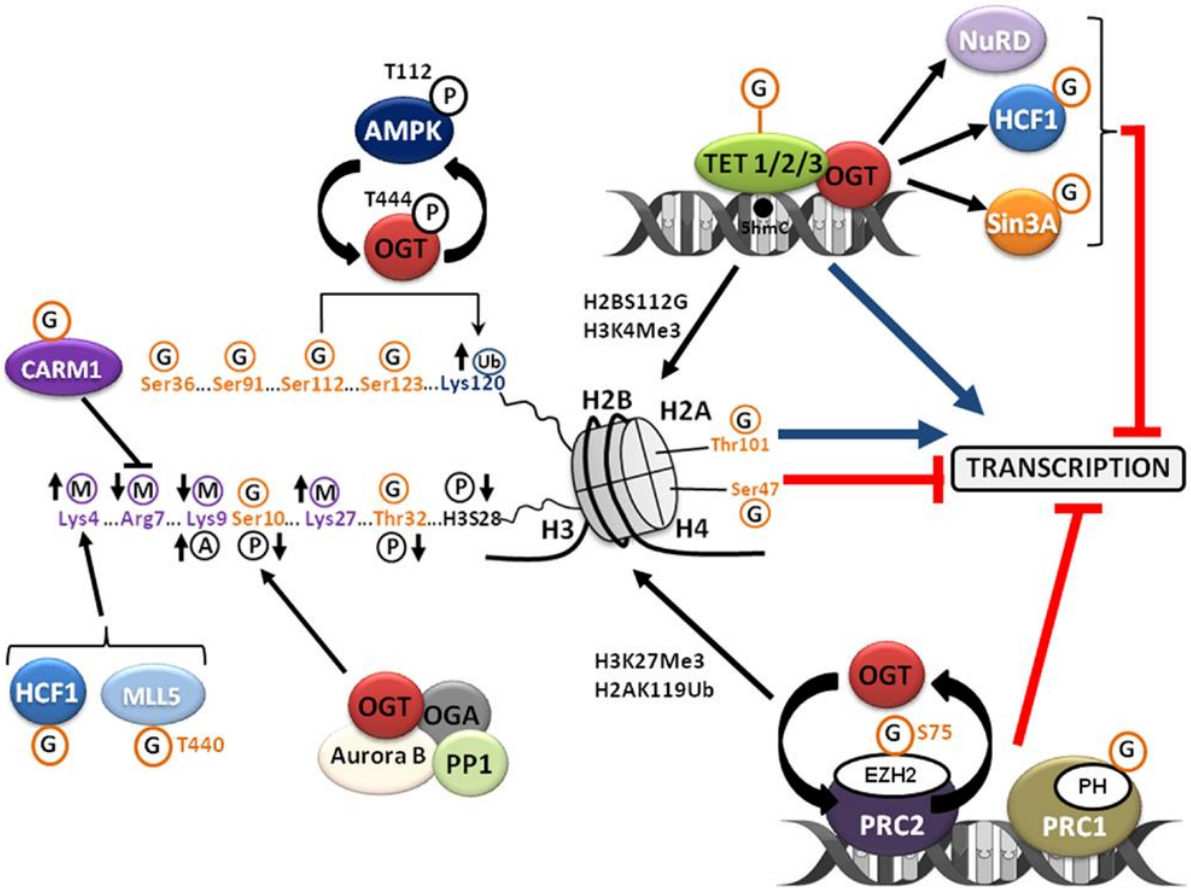

Vanessa Dehennaut1,2, Dominique Leprince2 ,O-GlcNAcylation, an epigenetic mark. Focus on the histone code, TET family proteins, and polycomb group proteins; Front. Endocrinol., 26 September 2014 | http://dx.doi.org/10.3389/fendo.2014.00155

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Tet 2

- Tet2 is upregulated after LPS stimulation
- Tet 2 represses myeloid leukaemia
- Tet2-deficient BMDC (bone marrow-derived dendritic cells), macrophages and Tet2-silenced human dendritic cells
- IL-6 mRNA expression was higher in the late phase (after 8h) of LPS stimulation

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- IL-6 protein levels also increased in the knock-out cells
- In contrary TNF-α mRNA levels did not increase
- Silencing of Tet3 hardly altered IL-6 expression

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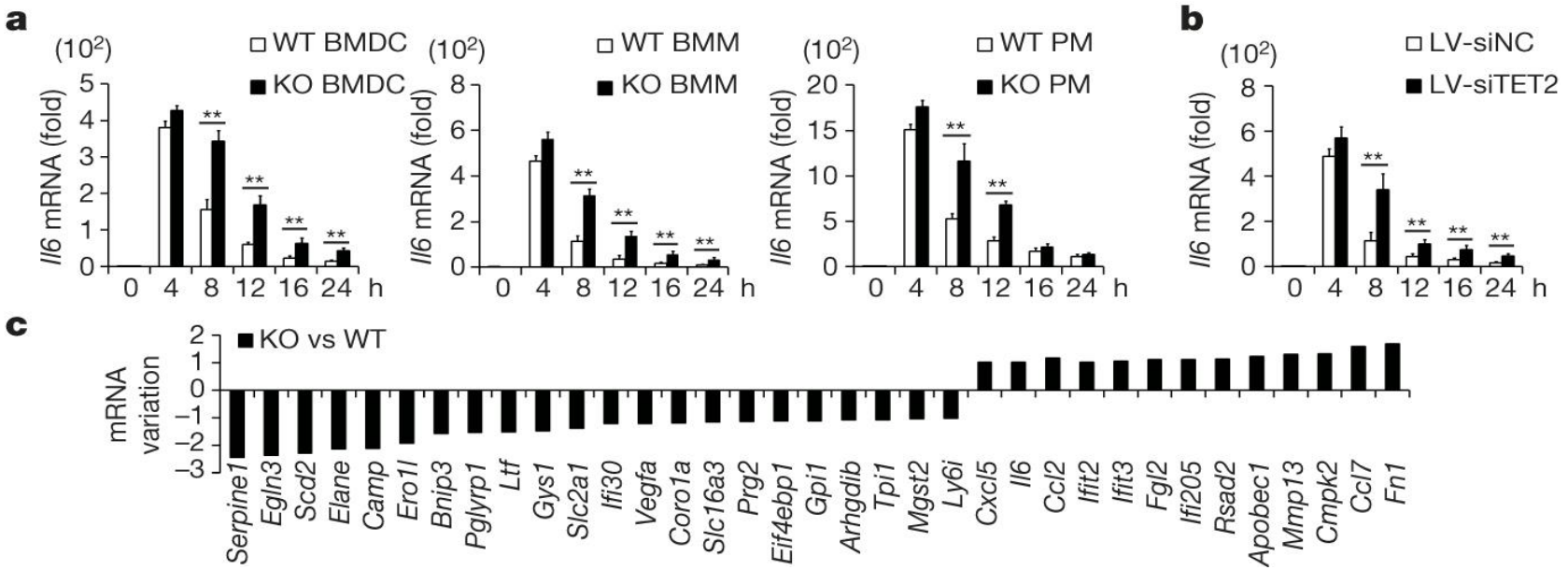

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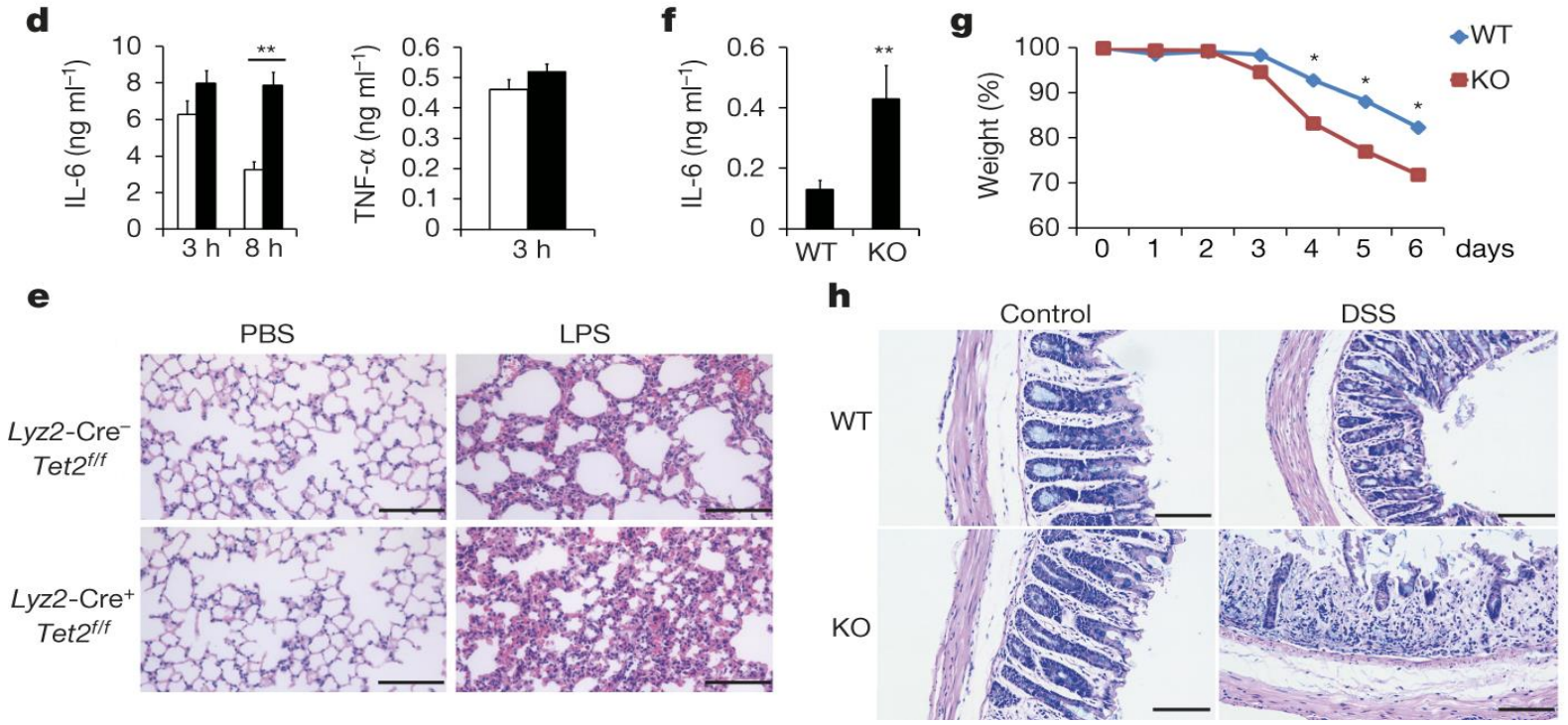

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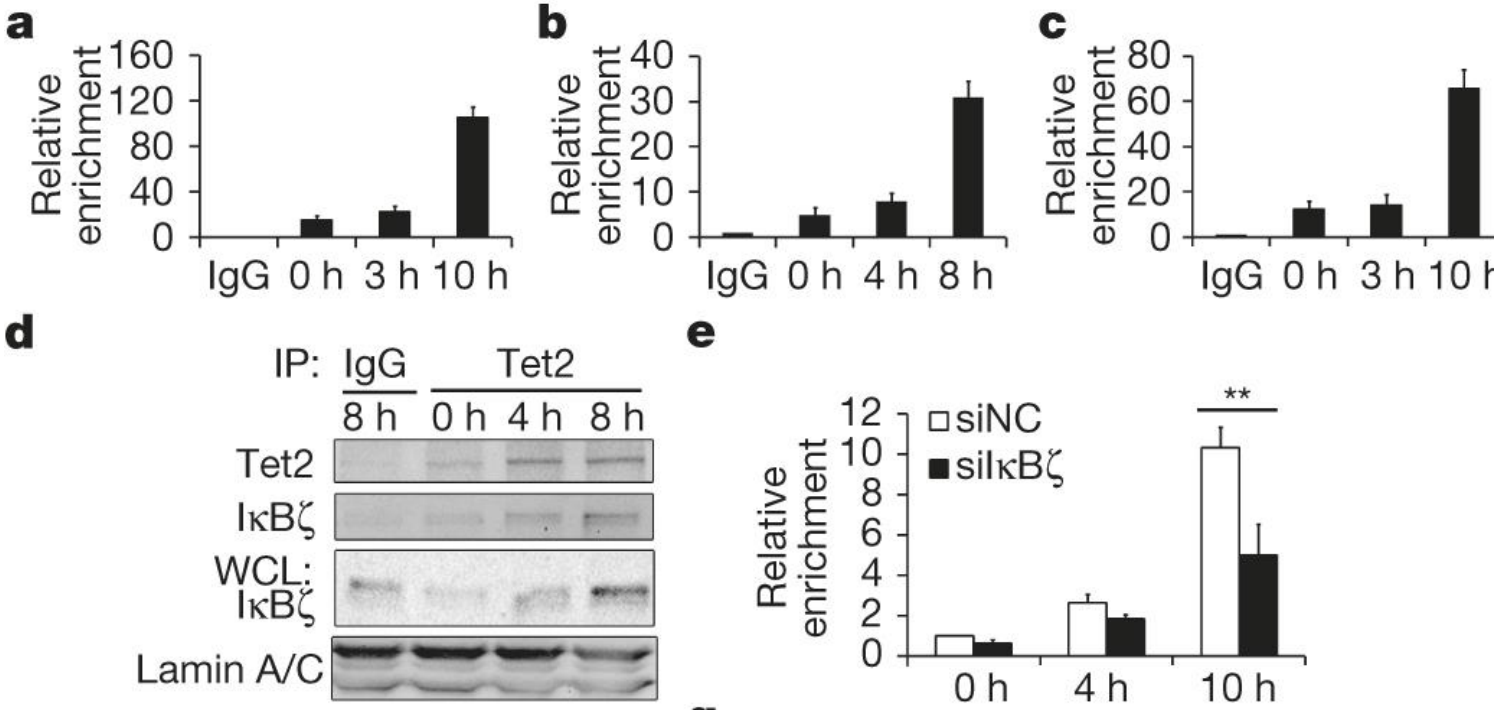

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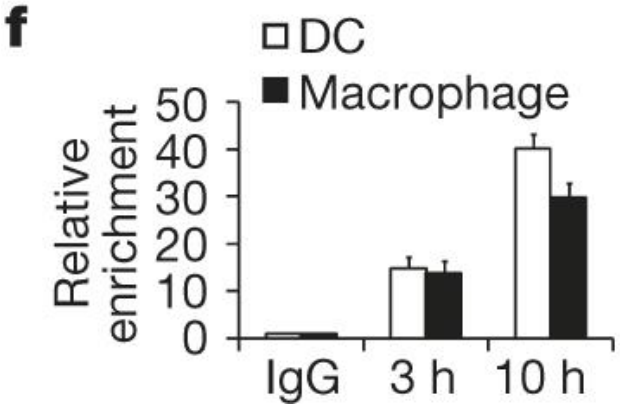

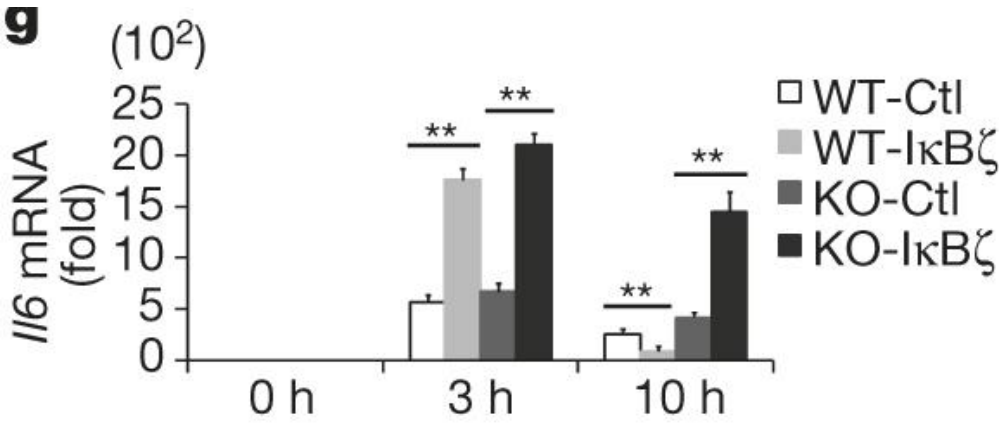

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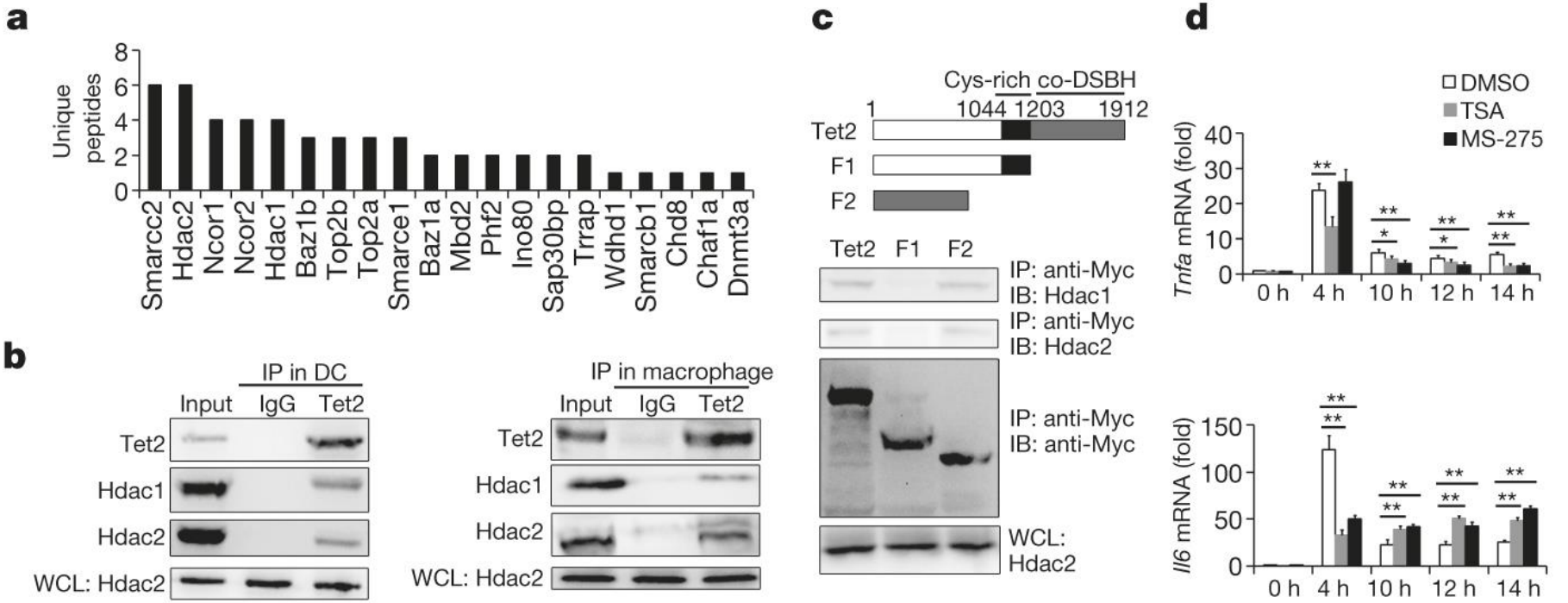

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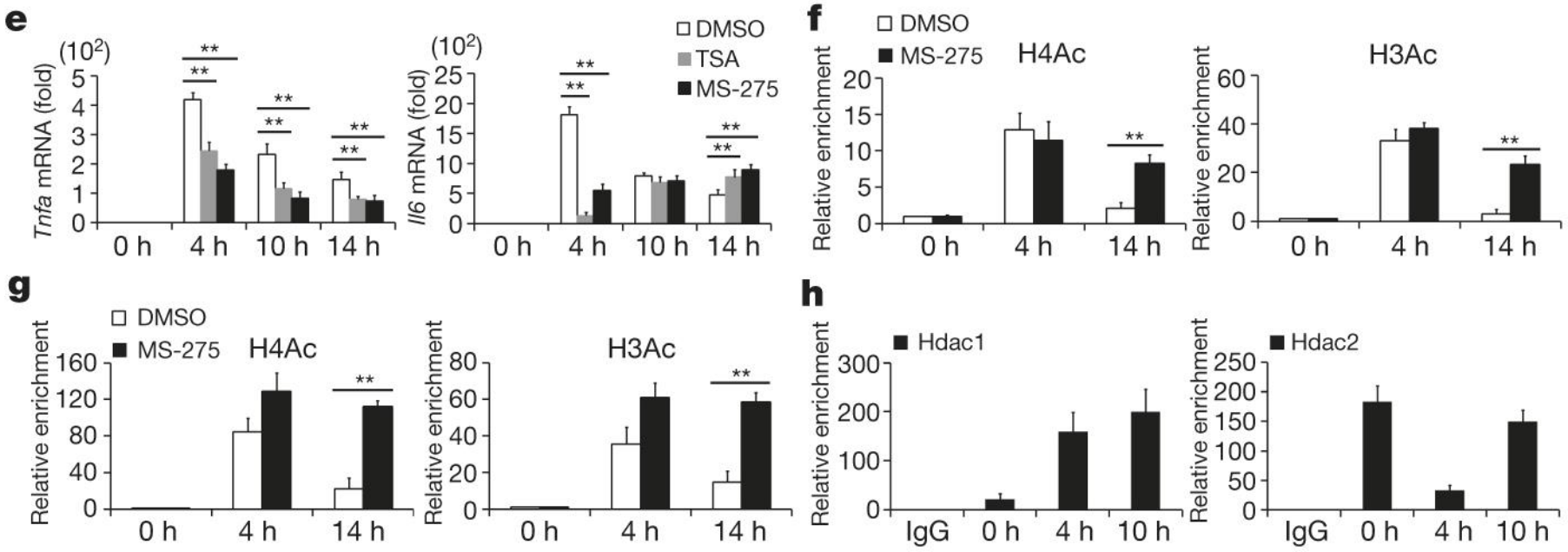

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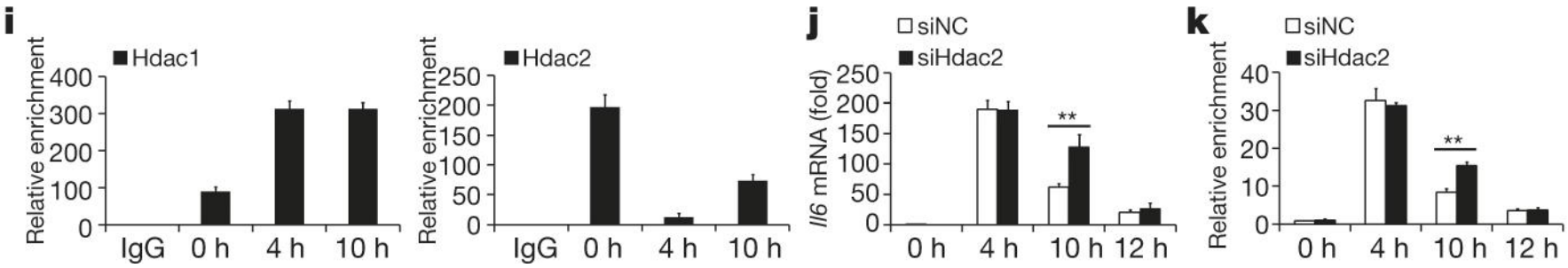

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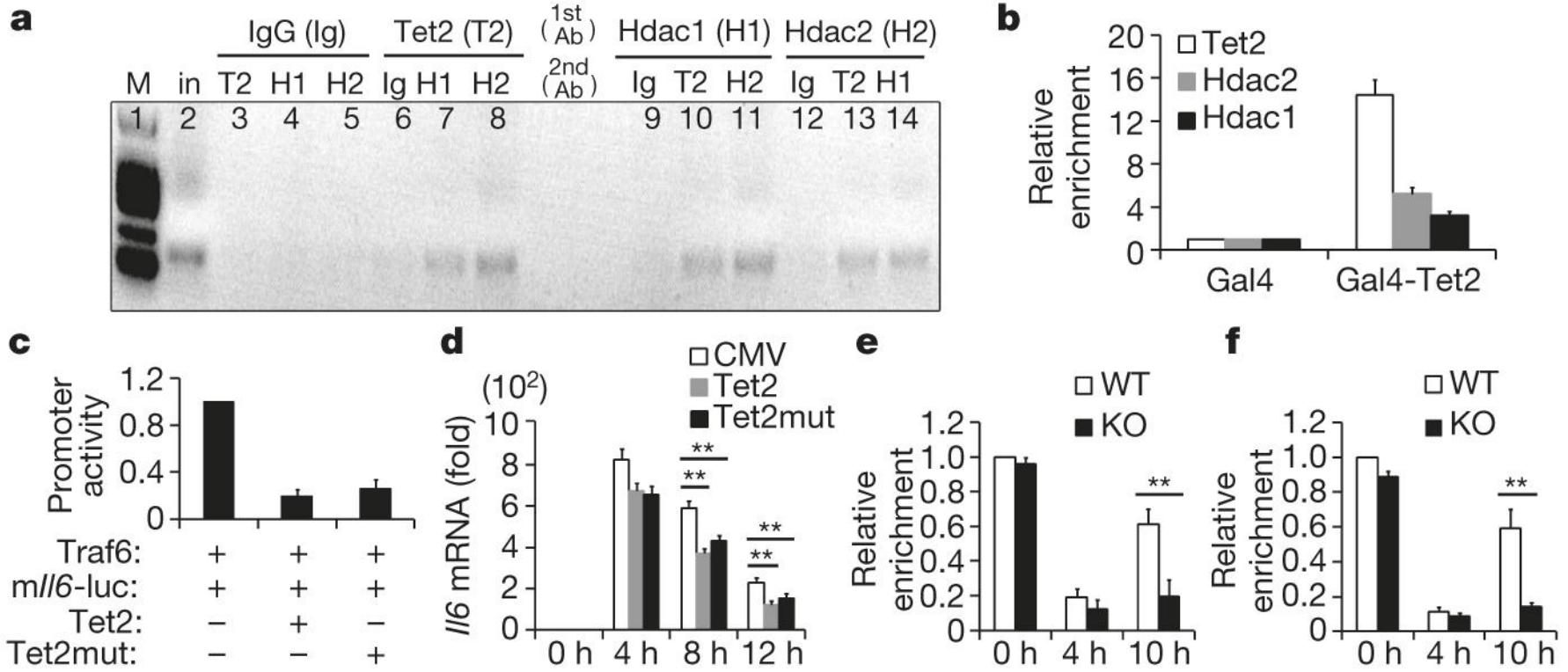

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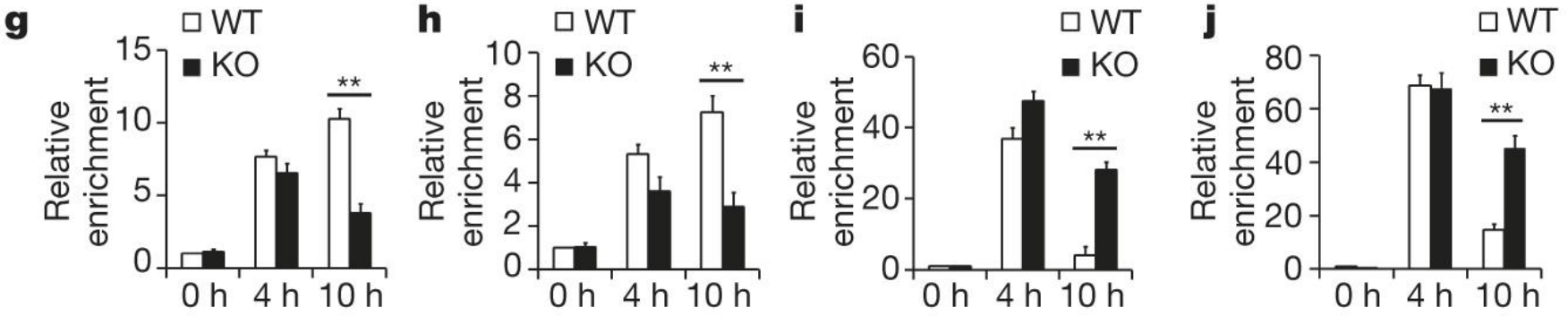

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Results

- Tet2 role in myeloid malignancies already known
- Discovered potential role in the regulation of imflammation
- Possible target in treatment of inflammation, autoimmunity and cancer

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Thank you for your attention!

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