

Highlights from EHA

Report dei gruppi di lavoro >>
[Disordini mieloproliferativi cronici]

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27-28 ottobre 2008

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Gruppo di lavoro

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[Disordini mieloproliferativi cronici]

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Key Questions in Myeloproliferative Neoplasms

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Biological key questions

1. What genetic event preceding or concomitant to *JAK2* V617F mutation contributes to MPN (*JAK2* negative)?
2. What are the molecular bases for the differences in the in vivo phenotypes induced by *JAK2* V617F?
3. Mechanism for constitutive mobilization of CD34+ cells in PMF
4. Mechanism for constitutive mobilization of endothelial progenitor cells and angiogenesis in PMF
5. Role of TGF beta in myelofibrosis and myeloproliferation of PMF

Operational (Clinical) key questions

1. *JAK2* mutation load and prognosis
2. Definition of resistance to HU in PV and PMF
3. Definition of response in ET/PV

Therapeutic key questions

1. Efficacy of molecularly targeted therapies
2. Clonal response in MPNs
3. Optimization of conventional therapies (Hct levels in PV?)

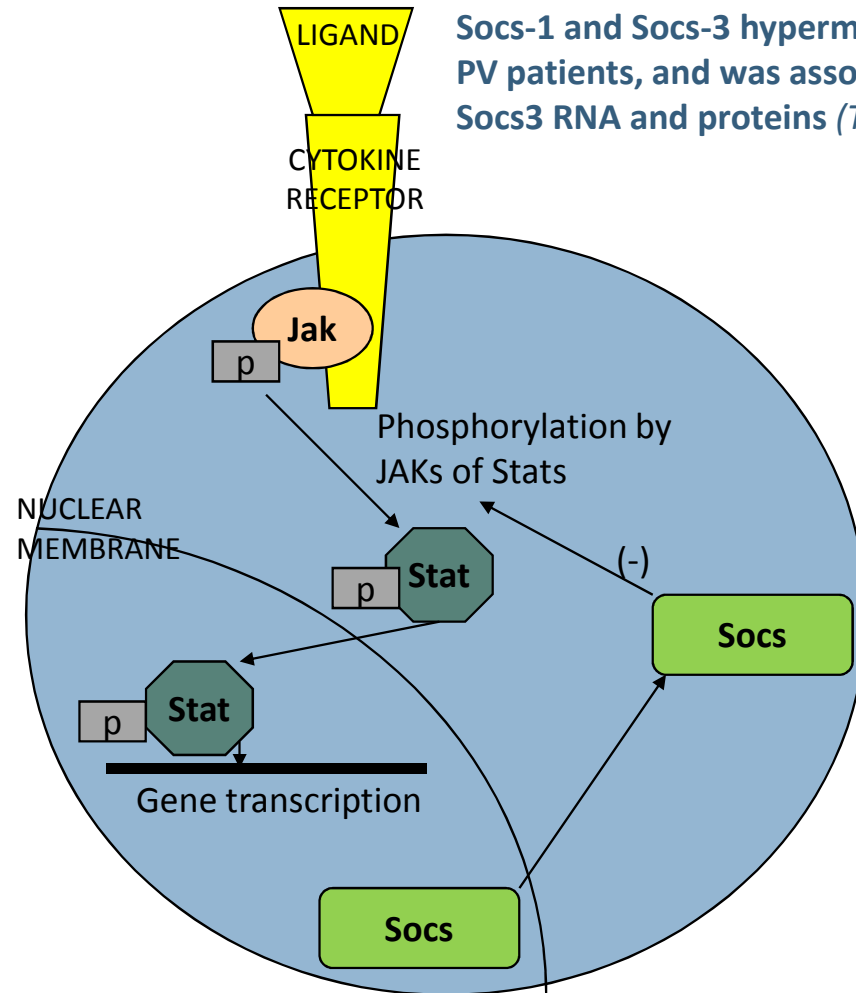
Biological questions

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Besides JAK2 V617 (and other mutations),
the phenotype may be determined by:

- SOCS
- Genomic instability
- miRNA
- CXCR4

Other JAK2-independent molecular events influence the phenotype of MPNs



Socs-1 and Socs-3 hypermethylation was detected in 23 out of 81 ET or PV patients, and was associated with significant reduction of Socs1 and Socs3 RNA and proteins (*Teofili et al, Int J Cancer, 2008*)

Socs: Suppressor of Cytokine Signaling

- CIS (cytokine inducible SH2 domain protein)
- Socs 1-7

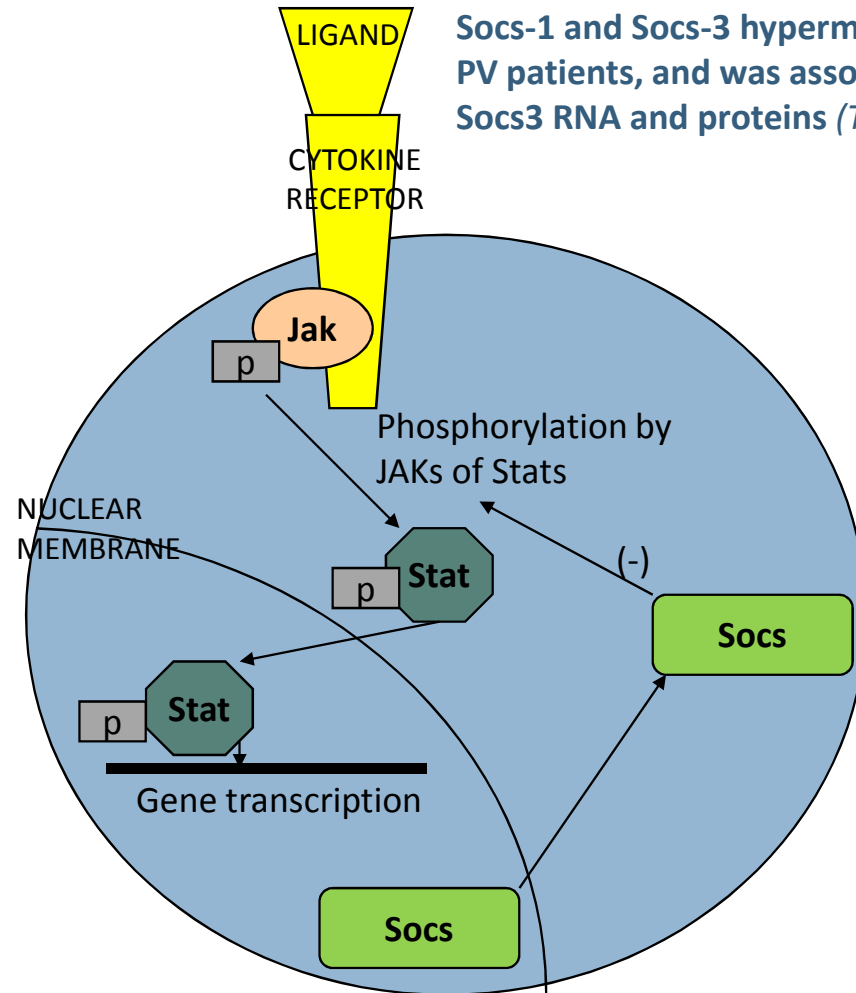
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JAK2 V617F and thrombosis

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Arterial thrombosis

- Leukocytosis
- Leukocyte function (activation)

Venous thrombosis

- Endothelial cells (?)

Clinical relevance of the association between JAK2 V617F allele load and evolution (thrombosis, leukemia, myelofibrosis)

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- New prognostic score for thrombosis? (need of a clinical trial – Hydroxyurea? Interferon? JAK2 inhibitors? Double anti-aggregation?)
- More therapy for high JAK2 V67F burden patients? (Which therapy?)

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Discussione