

CURRICULUM VITAE

NAME: Stefan N. CONSTANTINESCU, Prof., M.D., Ph.D.

POSITIONS:

2009- Member, Ludwig Institute for Cancer Research
 2008- (Part-time) Professor at the *Université catholique de Louvain*, Brussels, Belgium.
 2005- Associate Member, Ludwig Institute for Cancer Research, Brussels, Belgium.
 2003- Tenured Investigator of the FNRS (*Fonds National de la Recherche Scientifique*)
 2003- (Part-time) Associate Professor at the *Université catholique de Louvain*, Brussels, Belgium.
 2003 Member, Christian de Duve Institute of Cellular Pathology, Brussels, Belgium.
 2000- Associate Member, Christian de Duve Institute of Cellular Pathology, Brussels, Belgium.
 2000- Group Leader, Ludwig Institute for Cancer Research, Brussels Branch of Cancer Genetics, Brussels, Belgium.
 2000- Member of the Doctoral School of Genetics and Immunology (GIM), Mentor for Graduate Studies, *Université catholique de Louvain*, Brussels, Belgium.
 1995-2000 Anna Fuller Fellow in Molecular Oncology (1995-1998) & Postdoctoral Fellow of the The Medical Foundation, Boston (1998-2000), Whitehead Institute for Biomedical Research, Massachusetts Institute of Technology, Cambridge, MA (with Prof. Harvey F. Lodish)
 1992-1994 Postdoctoral Research Associate, Department of Pathology, University of Tennessee, Memphis College of Medicine (with Prof. Lawrence M. Pfeffer), Memphis, TN, U.S.A.
 1990-1992 Junior Lecturer, Departments of Cell Biology and Virology, University of Medicine and Pharmacy, Bucharest, and Research Associate, "Stefan S. Nicolau" Institute of Virology, Bucharest, Romania.

PROFESSIONAL ADDRESS:

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DATE AND PLACE OF BIRTH: June 6, 1964, Bucharest, Romania

NATIONALITY: Romanian and Belgian

CIVIL STATUS: Married, three children

EDUCATION/TRAINING: University of Medicine and Pharmacy, Carol Davilla Bucharest, Romania – M.D. in Medicine, 1988.

University of Medicine and Pharmacy, Carol Davilla Bucharest, Romania – Ph.D. in Virology, 1991.
Equivalence, *Catholic University of Louvain*, Doctor in Biomedical Sciences, Belgium, 2002.

TEACHING TASKS:

Since 2003, *Biologie Moléculaire des Régulations Hormonales* (BCMM2140), 30h together with Prof. Frédéric Lemaigre.

MASTER DEGREE STUDENTS SUPERVISION:

- 2001-2002 : Nadine Seubert, Mémoire de Licence en Sciences Biomédicales, Université de Wuerzburg

MD STUDENTS SUPERVISION:

- 2002-2006 : Yohan Royer, Doctorat en Sciences Biomédicales, UCL
- 2003-2007 : Judith Staerk, Doctorat en Sciences Biomédicales, UCL
- 2004- : Alexandra Dusa, Doctorat en Sciences Biomédicales, UCL
- 2007- : Jean-Michel Heine, Doctorat en Sciences Biomédicales, UCL (interrompu)
- 2007- : Roxana-Irina Albu, Doctorat en Sciences Biomédicales, UCL

PhD STUDENT SUPERVISION:

- 2002-2005 : Katharina Kubatzky, *Max-Planck Institute*, Freiburg, Germany
- 2002-2004 : Virginie Moucadel, CNRS, Marseille, France
- 2005-2007 : Carmen Diaconu, *Stefan S. Nicolau Institute of Virology*, Bucharest, Romania
- 2005- : Christian Pecquet, *Université d'Amiens*, France
- 2005- : Michael Girardot, *Université de Bordeaux II*, France
- 2007- : Nancy Caceres, *Université catholique de Louvain*, Belgium
- 2007- : Jhansi Kota, *Ludwig Institute* and *Karolinska Institute*, Stockholm, Sweden

MEMBER OF THE REVIEW COMMITTEE OF SCIENTIFIC JOURNALS:

- *Section Editor* for the *Signal Transduction* section, *Leukemia (The Journal of Normal and Malignant Hemopoiesis)*, since 2006;
- *Editorial Board Member*, *Journal of Cellular and Molecular Medicine*.

SCIENTIFIC COMMITTEES:

- | | |
|------|---|
| 2002 | Member, <i>Scientific Advisory Board</i> , <i>Institute of Bioinformatics</i> (in collaboration with Dr. Akhilesh Pandey, Johns Hopkins University, Baltimore, MD), Bangalore, India. |
| 2007 | Chair, <i>Scientific Advisory Board</i> , <i>Stefan S. Nicolau Institute of Virology</i> , Academy of Romania, Bucharest, Romania. |
| 2010 | Member, Scientific Program Committee for EHA (European hematology Association) Meeting 2011 (EHA 16), London. |

HONORS AND AWARDS:

- 2009- Corresponding Member, Academy of Medical Sciences of Romania
 2004- Corresponding Member, *Académie Européenne des Sciences, Lettres et Beaux-Arts*, Paris (France)
 2003 Maggy and Robert de Hovre Award in Immunology (*Fondation Maggy et Robert de Hovre*, Brussels, Belgium)
 1998 The Medical Foundation Fellowship, Boston (U.S.A.)
 1995-1998 Anna Fuller Fellow in Molecular Oncology, award shared between the M.I.T. Center for Cancer Research and the Boyer Center of the University de Yale (U.S.A.)
 1991 Prize of the Romanian Academy

PROFESSIONAL SOCIETIES:

- 2002- International Member, *American Society of Hematology*.
 2001- Member, *American Association for the Advancement of Science* (AAAS), Washington DC (U.S.A.).
 2000- Member, Advisory Board, ASPERA Educational Foundation, Boston, MA (U.S.A.).

OTHER ACTIVITIES:

- 2000-2002 Founding consultant, Therascope AG, Heidelberg, Germany (later Allantos, US, now Amgen).
 2002- Professor of Molecular Medicine, Faculty of Medicine, Carol Davilla University of Medicine and Pharmacy (<http://www.univermed-cdgm.ro/?pid=216>, 20-25h/year, since 2002, optional course in Molecular Medecine for the students of the Faculty of Medicine, Bucharest, Romania)
 2003- Expert Evaluator, European Commission.
 2003- International Member, *American Society of Hematology*.
 2008- Jury Member, European Research Council Advanced Grants

PUBLICATIONS

RESEARCH ARTICLES:

1990-1993

Patrascu I.V., **Constantinescu S.N.** & Dublanchet A. (1990) HIV-1 infection in Romanian children. *Lancet*. **335**(8690): 672.
IF : 10,232 (2000).

Cernescu C., **Constantinescu S.N.** & Patrascu I.V. (1990) Measles antibodies in HIV-1 infected children. *Rev. Roum. Virol.* **41**(2): 133-134.

Cernescu C., **Constantinescu S.N.** & Popescu L.M. (1990) Electron microscopic observations of vesicular stomatitis virus particles penetration in human fibroblasts. *Rev. Roum. Virol.* **41**(2): 93-96.

Constantinescu S.N., Cernescu C., Balta, F., Maniu, H. & Popescu, L.M. (1990). The priming effect of human interferon is mediated by protein kinase C. *J. Interferon Res.* **10**(6): 589-597.

Constantinescu S.N., Cernescu C. & Popescu L.M. (1991) Effects of protein kinase C inhibitors on viral entry and infectivity. *FEBS Letters* **292**(1-2): 31-33.
IF : 3,440 (2000).

Wang C., **Constantinescu S.N.**, MacEwan D.J., Strulovici B., Decker L.V., Parker P.J. & Pfeffer L.M. (1993). Interferon- α induces PKC- ϵ gene expression and a 4.7 kb PKC- ϵ -related transcript. *Proc. Natl. Acad. Sci. U.S.A.* **90**(15): 6944-6948.
IF : 10,789 (2000).

1994

Constantinescu S.N., Croze E., Wang C., Murti A., Basu L., Mullersman J. & Pfeffer L. M. Role of the IFN- α/β receptor chain 1 in structure and transmembrane signaling of the IFN α/β receptor complex. *Proc. Natl. Acad. Sci. U.S.A.* **91**(20): 9602-9606, 1994.
IF : 10,789 (2000).

Colamonici O.R., Porterfield B., Domanski P., **Constantinescu S.N.** & Pfeffer L.M. Complementation of the interferon α response in resistant cells by expression of the cloned subunit of the interferon- α receptor: A central role of this subunit in IFN- α signaling. *J. Biol. Chem.* **269**: 9698-9602, 1994.
IF : 7,368 (2000).

1995

Constantinescu S.N., Croze E., Murti A., Wang C., Basu L., Hollander D., Russell-Harde D., Betts M., Garcia-Martinez V., Mullersman J.E. & Pfeffer L.M. Expression and signaling specificity of the IFNAR chain of the type I IFN receptor complex. *Proc. Natl. Acad. Sci. U.S.A.* **92**(23): 10487-10491, 1995.
IF : 10,789 (2000).

1996

Yang C.H., Shi W., Basu L., Murti A., **Constantinescu S.N.**, Blatt L., Croze E., Mullersman J.E. & Pfeffer L. M. Direct association of STAT3 with the IFNAR1 signal transducer chain of the type I IFN receptor. *J. Biol. Chem.* **271**(14): 8057-8061, 1996.
IF : 7,368 (2000).

Pfeffer L.M., Wang C., **Constantinescu S.N.**, Croze E., Blatt L.M., Albino A.P. & Nanus D.M. Human renal cancers resistant to IFN's antiproliferative action exhibit sensitivity to IFN's gene-inducing and antiviral actions. *J. Urol.* **156**(5): 1867-1871, 1996.
IF : 2,896 (2000).

1997

Liu X., Sun Y., **Constantinescu S.N.**, Karam E., Weinberg R.A. & Lodish H.F. Transforming growth factor α -induced phosphorylation of Smad3 is required for growth inhibition and transcriptional induction in epithelial cells. *Proc. Natl. Acad. Sci. U.S.A.* **94**(20): 10669-10674, 1997.
IF : 10,789 (2000).

Holland K.E., Owczarek C.M., Hwang S.Y., Tymms M.J., **Constantinescu S.N.**, Pfeffer L.M. & Hertzog P.J. A type I interferon signaling factor, ISF21, encoded on chromosome 21 is distinct from receptor components and their down-regulation and is necessary for transcriptional activation of IFN regulated genes. *J. Biol. Chem.* **272**(34): 21045-21051, 1997.
IF : 7,368 (2000).

1998

Basu L., Yang C.H., Murti A., Garcia-Martinez V., Croze E., **Constantinescu S.N.**, Mullersman J.E. & Pfeffer L.M. The antiviral action of interferon is potentiated by removal of the conserved IRTAM domain of the IFNAR1 chain of the interferon α/β receptor: Effects on STAT activation and receptor down-regulation. *Virology.* **242**(1): 14-21, 1998.
IF : 3,507 (2000).

Constantinescu S.N., Wu H., Liu X., Beyer W., Fallon A. & Lodish H.F. The anemic Friend Virus gp55 envelope protein induces erythroid differentiation in fetal liver CFU-E's. *Blood.* **91**(4): 1163-1172, 1998.
IF : 8,977 (2000).

1999

Constantinescu S.N., Liu X., Beyer W., Fallon A., Shekar S., Henis Y.I., Smith S.O. & Lodish H.F. Activation of the erythropoietin receptor by the gp55-P Viral envelope protein is determined by a single amino acid in its transmembrane domain. *EMBO J.* **18**(12): 3334-3347, 1999.
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2000

Liu X., **Constantinescu S.N.**, Bogan J., Hirsch D. & Lodish H.F. Quantitative expression of genes at predetermined levels using bicistronic retroviral vectors. *Anal. Biochem.* **280**(1): 20-28, 2000.
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2001

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Huang L.J., **Constantinescu S.N.** & Lodish H.F. The N-terminal domain of Janus kinase 2 is required for cell-surface expression of erythropoietin and prolactin receptors. *Mol. Cell*, **8**(6): 1327-1338, 2001.

IF : 16,611.

2002

Pandey A., Ibarrola N., Kratchmarova I., Fernandez M.M., **Constantinescu S.N.**, Ohara O., Sawadikosol S., Lodish H.F. & Mann M. A novel Src homology 2 domain-containing molecule, Src-like adapter protein-2 (SLAP-2), which negatively regulates T cell receptor signaling. *J. Biol. Chem.* **277**(21): 19131-19138, 2002.

IF : 6,696.

Lejeune D., Dumoutier L., **Constantinescu S.N.**, Kruijjer W., Schuringa J.J. & Renauld J.-C. IL-22 activates the JAK/STAT, ERK, JNK and p38 MAP kinase pathways in a rat hepatoma cell line: shared and distinct pathways from IL-10. *J. Biol. Chem.* **277**: 33676-33682, 2002.

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2003

Peri S., Navarro J.D., Amanchy R., Kristiansen T.Z., Jonnalagadda C.K., Surendranath V., Niranjana V., Muthusamy B., Gandhi T.K., Gronborg M., Ibarrola N., Deshpande N., Shanker K., Shivashankar H.N., Rashmi B.P., Ramya M.A., Zhao Z., Chandrika K.N., Padma N., Harsha H.C., Yatish A.J., Kavitha M.P., Menezes M., Choudhury D.R., Suresh S., Ghosh N., Saravana R., Chandran S., Krishna S., Joy M., Anand S.K., Madavan V., Joseph A., Wong G.W., Schiemann W.P., **Constantinescu S.N.**, Huang L., Khosravi-Far R., Steen H., Tewari M., Ghaffari S., Blobel G.C., Dang C.V., Garcia J.G., Pevsner J., Jensen O.N., Roepstorff P., Deshpande K.S., Chinnaiyan A.M., Hamosh A., Chakravarti A. & Pandey A. Development of human protein reference database as an initial platform for approaching systems biology in humans. *Genome Res.* **13**(10): 2363-2371, 2003.

IF : 9,635.

Constantinescu S.N., Keren T., Russ W.P., Ubarretxena-Belandia I., Malka Y., Kubatzky K., Engelman D. M., Lodish H.F. & Henis Y.I. (2003) The Epo receptor transmembrane protein modulates complex formation with viral anemic and polycythemic gp55 proteins. *J. Biol. Chem.* **278**(44): 43755-43763, 2003.

IF : 6,482.

Seubert N., Royer Y., Staerk J., Kubatzky K.F., Moucadel V., Krishnakumar S., Smith S.O. & **Constantinescu S.N.** Active and inactive orientations of the transmembrane and cytosolic domains of the erythropoietin receptor dimer. *Mol. Cell.* **12**(5): 1239-1250, 2003.

IF : 16,835.

2004

Royer Y., Menu C., Liu X. & **Constantinescu S.N.** High-throughput Gateway bicistronic retroviral vectors for stable expression in mammalian cells: exploring the biologic effects of STAT5 overexpression. *DNA Cell Biol.* **23**(6): 355-365, 2004.
IF : 2,398.

2005

Kubatzky K.F., Liu W., Goldgraben K., Simmerling C., Smith S.O. & **Constantinescu S.N.** Structural requirements of the extracellular to transmembrane domain junction for erythropoietin receptor function. *J. Biol. Chem.* **280**(15): 14844-14854, 2005.
IF : 5,854.

Moucadel V. & **Constantinescu S.N.** Differential STAT5 signaling by ligand-dependent and constitutively active cytokine receptors. *J. Biol. Chem.* **280**(14): 13364-13373, 2005.
IF : 5,854.

Liu W., Crocker E. & **Constantinescu S. N.** Helix packing and orientation in the transmembrane dimer of gp55-P of the Spleen Focus Forming Virus. *Biophys. J.* **89**(2): 1194-1202, 2005.
IF : 4,507.

Royer Y., Staerk, J., Costuleanu M., Courtoy P.J. & **Constantinescu S.N.** Janus kinases affect thrombopoietin receptor cell surface localization and stability. *J. Biol. Chem.* **280**(29): 27251-27261, 2005.
IF : 5,854.

James C., Ugo V., Le Couedic J.-P., Staerk J., Delhommeau F., Lacout C., Garcon L., Raslova H., Berger R., Bennaceur-Griscelli A., Villeval J.-L., **Constantinescu S.N.**, Casadevall N. & Vainchenker W. A unique clonal JAK2 mutation leading to constitutive signalling causes polycythaemia vera. *Nature.* **434**(7037): 1144-1148, 2005.
IF : 29,273.

Staerk J., Kallin A., Demoulin J.-B., Vainchenker W. & **Constantinescu S.N.** JAK1 and Tyk2 Activation by the homologous Polycythemia Vera JAK2 V617F mutation: Cross Talk with IGF1 Receptor *J. Biol. Chem.* **280**(51): 41893-41899, 2005.
IF : 5,854.

2006

Sato T., Kienlen-Campard P., Ahmed M., Liu W., Li H., Elliott J.I., Aimoto S., **Constantinescu S.N.**, Octave J.-N. & Smith S.O. Inhibitors of amyloid toxicity based on beta-sheet packing of Abeta40 and Abeta42. *Biochemistry.* **45**(17): 5503-5516, 2006.
IF : 3,633.

Staerk J., Lacout C., Sato T., Smith S.O., Vainchenker W. et **Constantinescu S.N.** An amphipathic motif at the transmembrane-cytoplasmic junction prevents autonomous activation of the thrombopoietin receptor. *Blood.* **107**(5): 1864-1871, 2006.
IF : 10,370.

2007

Staerk J., Kallin A., Royer Y., Diaconu C.C., Dusa A., Demoulin J.-B., Vainchenker W. & **Constantinescu S.N.** JAK2, the JAK2 V617F mutant and cytokine receptors. *Pathol. Biol. (Paris).* **55**(2): 88-91, 2007.

IF : 0,953.

Hookham M.B., Elliott J., Suessmuth Y., Staerk J., Ward A.C., Vainchenker W., Percy M.J., McMullin M.F., **Constantinescu S.N.** & Johnston J.A. The myeloproliferative disorder-associated JAK2 V617F mutant escapes negative regulation by suppressor of cytokine signaling 3. *Blood*. **109**(11): 4924-4929, 2007.

IF : 10,896.

2008

Tefferi A. & **Constantinescu S.N.** Introduction to 'A special spotlight review series on BCR-ABL-negative myeloproliferative neoplasms'. *Leukemia*. **22**(1): 1-1, 2008.

IF : 8,634.

Knoops L., Hornakova T., Royer Y., **Constantinescu S.N.** & Renault J.-C. JAK kinases overexpression promotes in vitro cell transformation. *Oncogene*. **27**(11): 1511-1519, 2008.

IF : 7,216.

Wernig G., Gonneville J.R., Crowley B.J., Rodrigues M.S., Reddy M.M., Hudon H.E., Walz C., Reiter A., Podar K., Royer Y., **Constantinescu S.N.**, Tomasson M.H., Griffin J.D., Gary Gilliland D. & Sattler M. The Jak2V617F oncogene associated with myeloproliferative diseases requires a functional FERM domain for transformation and for expression of the Myc and Pim proto-oncogenes. *Blood*. **111**(7): 3751-3759, 2008.

IF : 10,432.

Dusa A., Staerk J., Elliott J., Pecquet C., Poirel H.A., Johnston J.A. & **Constantinescu S.N.** Substitution of JAK2 V617 by large non-polar amino acid residues causes activation of JAK2. *J. Biol. Chem.* **283**(19): 12941-12948, 2008.

IF : 5,520.

Lee Y., Hyung S.W., Jung H.J., Kim H.J., Staerk J., **Constantinescu S.N.**, Chang E.J., Lee Z.H., Lee S.W. & Kim H.H. The ubiquitin-mediated degradation of Jak1 modulates osteoclastogenesis by limiting interferon- induced inhibitory signaling. *Blood*. **111**(2): 885-893, 2008.

IF : 10,432.

Flex E., Petrangeli V., Stella L., Chiaretti S., Hornakova T., Knoops L., Ariola C., Fodale V., Clappier E., Paoloni F., Martinelli S., Fragale A., Sanchez M., Tavolaro S., Messina M., Cazzaniga G., Camera A., Pizzolo G., Tornesello A., Vignetti M., Battistini A., Cavé H., Gelb B.D., Renault J.-C., Biondi A., **Constantinescu S.N.**, Foà R. & Tartaglia M. Somatically acquired JAK1 mutations in adult acute lymphoblastic leukemia. *J. Exp. Med.* **205**(4): 751-758, 2008.

IF : 15,463.

Kienlen-Campard P., Tasiaux B., Van Hees J., Li M., Huysseune S., Sato T., Fei J.Z., Aimoto S., Courtoy P.J., Smith S.O., **Constantinescu S.N.** & Octave J.-N. Amyloidogenic processing but not acid production requires a precisely oriented APP dimer assembled by transmembrane GXXXG motifs. *J. Biol. Chem.* **283**(12): 7733-7744, 2008.

IF : 5,520.

Knoops L., Hermans C., Ferrant A. & **Constantinescu S.N.** Clinical implications of JAK2 mutations in myeloproliferative disorders. *Acta Clin. Belg.* **63**(2): 93-98, 2008.

IF : 1,282.

Kumar K.G.S., Varghese B., Banerjee A., Baker D.P., **Constantinescu S.N.**, Pellegrini S. & Fuchs S.Y. Basal ubiquitin-independent internalization of interferon alpha receptor is prevented by Tyk2-mediated masking of a linear endocytic motif. *J. Biol. Chem.* **283**(27): 18566-18572, 2008.

IF : 5,520.

Gakovic M., Ragimbeau J., Francois V., **Constantinescu S.N.** & Pellegrini S. The Stat3-activating Tyk2 V678F mutant does not up-regulate signaling through the type I interferon receptor but confers ligand hypersensitivity to a homodimeric receptor. *J. Biol. Chem.* **283**(27): 18522-18529, 2008.

IF : 5,520.

Van Pelt K., Nollet F., Seileslag D., Knoops L., **Constantinescu S.N.**, Criel A. & Billiet J. The JAK2V617F mutation can occur in a hematopoietic stem cell that exhibits no proliferative advantage: a case of human allogeneic transplantation. *Blood.* **112**(3): 921-922, 2008.

IF : 10,432.

Malka Y., Hornakova T., Royer Y., Knoops L., Renaud J.-C., **Constantinescu S.N.** & Henis Y.I. Ligand-independent homomeric and heteromeric complexes between interleukin-2 or -9 receptor subunits and the gamma chain. *J. Biol. Chem.* **283**(48): 33569-33577, 2008.

IF : 5,520.

2009

Hornakova T., Staerk J., Royer Y., Flex E., Tartaglia M., **Constantinescu S.N.**, Knoops L. & Renaud J.-C. Acute lymphoblastic leukemia-associated JAK1 mutants activate the Janus kinase/STAT pathway via interleukin-9 receptor alpha homodimers. *J. Biol. Chem.* **284**(11): 6773-6781, 2009.

IF : 5,520 (2008).

Sato T., Tang T.C., Reubins G., Fei J.Z., Fujimoto T., Kienlen-Campard P., **Constantinescu S.N.**, Octave J.-N., Aimoto S. & Smith S.O. A helix-to-coil transition at the epsilon-cut site in the transmembrane dimer of the amyloid precursor protein is required for proteolysis. *Proc Natl Acad Sci U.S.A.* **106**(5): 1421-1426, 2009.

IF : 9,380 (2008).

Elliott J., Suessmuth Y., Scott L.M., Nahlik K., McMullin M.F., **Constantinescu S.N.**, Green A. R. & Johnston J.A. SOCS3 tyrosine phosphorylation as a potential bio-marker for myeloproliferative neoplasms associated with mutant JAK2 kinases. *Haematologica.* **94**(4): 576-580, 2009.

Marty C., Chaligné R., Lacout C., **Constantinescu S.N.**, Vainchenker W. & Villeval J.L. Ligand-independent thrombopoietin mutant receptor requires cell surface localization for endogenous activity. *J. Biol. Chem.* **284**(18): 11781-11791.

IF : 5,520 (2008).

Plo I., Zhang Y., Le Couédic J.-P., Nakatake M., Boulet J.-M., Itaya M., Smith S.O., Debili N., **Constantinescu S.N.**, Vainchenker W., Louache F. & de Botton S. An activating mutation in the CSF3R gene induces a hereditary chronic neutrophilia. *J. Exp. Med.* **206**(8): 1701-1707, 2009.

IF : 15,463 (2008).

2010

Pecquet C., Staerk J., Chaligné R., Goss V., Lee K.A., Zhang X., Rush J., Van Hees J., Poirel H.A., Scheiff J.M., Vainchenker W., Giraudier S., Polakiewicz R.D. & **Constantinescu S.N.** Induction of myeloproliferative disorder and myelofibrosis by thrombopoietin receptor W515 mutants is mediated by cytosolic tyrosine 112 of the receptor. *Blood.* **115**(5): 1037-1048, 2010.

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Kandasamy K., Mohan S.S., Raju R., Keerthikumar S., Kumar G.S., Venugopal A.K., Telikicherla D., Navarro J.D., Mathivanan S., Pecquet C., Gollapudi S.K., Tattikota S.G., Mohan S., Padhukasahasram

H., Subbannayya Y., Goel R., Jacob H.K., Zhong J., Sekhar R., Nanjappa V., Balakrishnan L., Subbaiah R., Ramachandra Y.L., Rahiman B.A., Prasad T.S., Lin J.X., Houtman J.C., Desiderio S., Renauld J.-C., **Constantinescu S.N.**, Ohara O., Hirano T., Kubo M., Singh S., Khatri P., Draghici S., Bader G.D., Sander C., Leonard W.J. & Pandey A. NetPath: a public resource of curated signal transduction pathways. *Genome Biol.* **11**(1): R3, 2010.

Girardot M., Pecquet, C., Boukour, S., Knoop, L., Ferrant, A., Vainchenker, W., Giraudier S. & **Constantinescu S.N.** miR-28 Is a thrombopoietin receptor targeting microRNA detected in a fraction of myeloproliferative neoplasm patient platelets. *Blood*. DOI 10.1182/blood-2008-06-165985 2010 (epubMay 5).

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REVIEW ARTICLES:

Pfeffer L.M., **Constantinescu S.N.** & Wang C. Transmembrane signaling by IFN- α . *Prog. Mol. Subcell. Biol.* **14**: 242-259, 1994.

Watowich S.S., Wu H., Socolovsky M., Klingmuller U., **Constantinescu S.N.** & Lodish H.F. Cytokine receptor signal transduction and the control of hematopoietic cell development. *Annu. Rev. Cell Dev. Biol.* **12**: 91-129, 1996.

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Constantinescu S.N. Stem cell generation and choice of fate: role of cytokines and cellular microenvironment. *J. Cell. Mol. Med.* **4**(4): 233-248, 2000.

Constantinescu S.N. Stemness, fusion and renewal of hematopoietic and stem cells. *J. Cell. Mol. Med.* **7**: 103-112, 2003.

Vainchenker W. & **Constantinescu S.N.** A unique activating mutation in JAK2 is at the origin of polycythemia vera and allows a new classification of myeloproliferative diseases. *Hematology (Am. Soc. Hematol. Educ. Program)*: 195-200, 2005.

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BOOK CHAPTERS

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Stefan N. CONSTANTINESCU studies the structure and function of the cytokine receptors, the JAK-STAT signalization and their implication in hematopoietic diseases such as myeloproliferative neoplasms. During his PhD studies in Virology at the University of Medicine and Pharmacy in Bucharest, he discovered an AIDS pediatric epidemic in Romania (*Lancet* 1990, 335, 672), which induced drastic changes in blood banking controls in Eastern Europe and elsewhere. Later, he studied the mechanism of induction action of type-I interferon, and together with Lawrence Pfeffer at the University of Tennessee, Memphis, he described the key function in signalization and tyrosine phosphorylation of the IFNAR1 subunit of the type I interferon receptor. During his stay in the Whitehead Institute and the M.I.T. (Cambridge, Massachusetts) in Prof. Harvey Lodish lab, he contributed to the elucidation of the activation mechanism of the erythropoietin receptor (*Molecular Cell* 2001), understood the function of chaperone for the JAK2 protein (*Molecular Cell* 2001) and discovered that the transmembrane sequence of the EpoR dimerizes (*Proc. Natl. Acad. Sci. USA* 2001) and becomes a specific target of the viral envelope proteins, which results in an activation of the receptor (*EMBO J* 1999). His research group at the Ludwig Institute and at the de Duve Institute (*Université catholique de Louvain*), contributed in collaboration with Dr William Vainchenker at Institut Gustave Roussy in Villejuif, France to the discovery of the *JAK2* V617F mutation in the human myeloproliferative diseases (*Nature* 2005, *J. Biol. Chem.* 2005,) and is actively investigating the mechanism by which a pseudokinase domain mutation activates the kinase domain (*J. Biol. Chem* 2008, *Plos One* 2010). The group also described similar activating mutations in JAK1 and Tyk2 (*J. Biol. Chem* 2005); such mutations were then described in acute human T leukemias (*J. Exp. Med.* 2008) Moreover, the group described an amphipathic motif, in the thrombopoietin receptor juxtamembrane region, which is necessary to maintain the receptor inactive in the absence of the ligand (*Blood* 2006). Mutations in TpoR in W515 of this motif are causing 3-10% of human myeloproliferative neoplasms that do not harbor the *JAK2* V617F mutation, and induce in vivo a very severe phenotype due to pathologic activation of MAP-kinase pathway via Tyr112 of TpoR (*Blood* 2010). The lab is also involved in proteomics and genomics studies in human cancers and also on more fundamental studies on the code which is at the basis of the specific interactions between transmembranes and juxtamembrane sequences and established a system to study the biological effects of the transmembrane proteins depending on their dimeric orientation (*Molecular Cell* 2003).