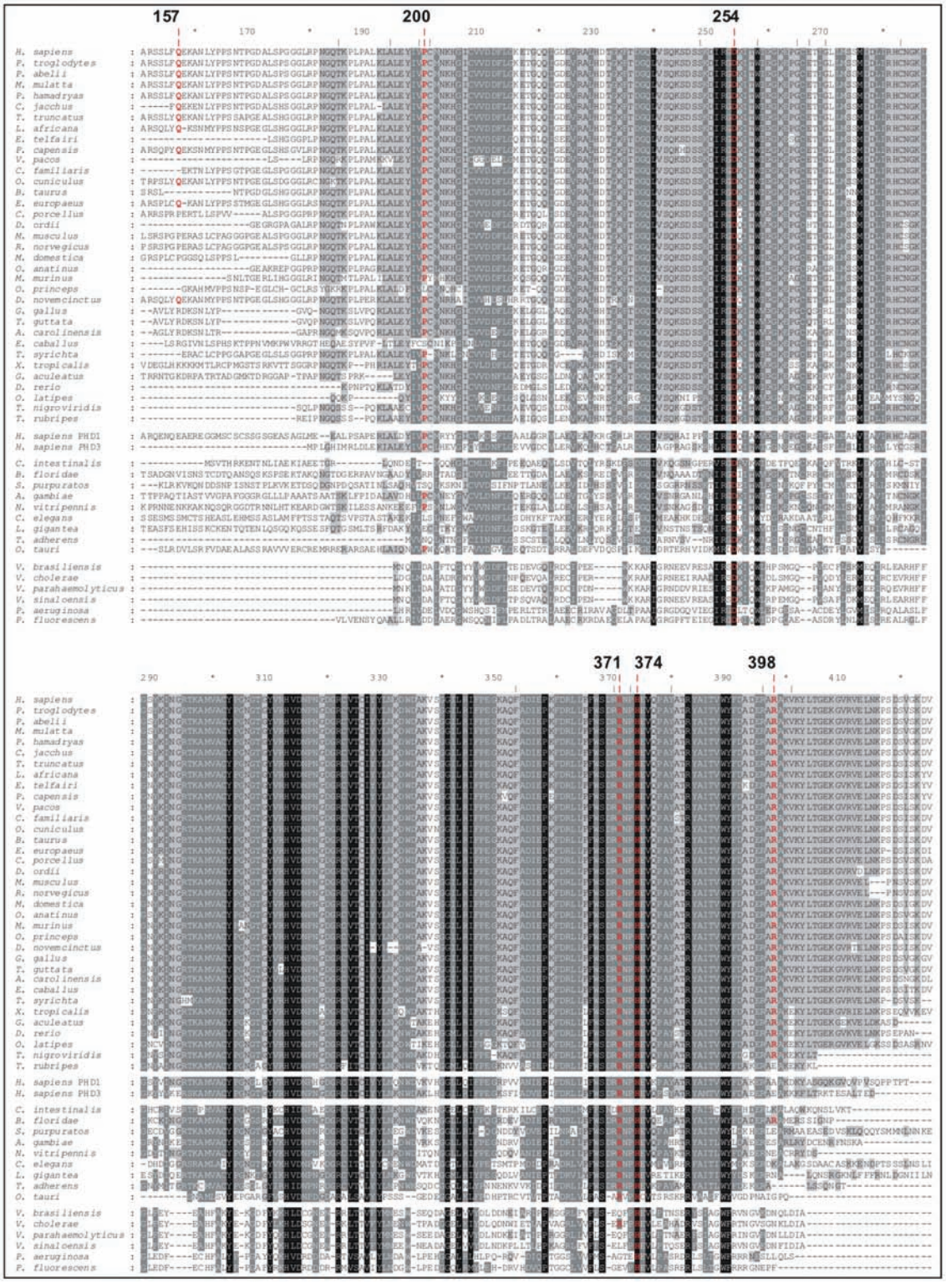
Distinct deregulation of the hypoxia inducible factor by *PHD2* mutants identified in germline DNA of patients with polycythemia

Charline Ladroue,[1]* David Hoogewijs,[2]* Sophie Gad,[1] Romain Carcenac,[1] Federica Storti,[2] Michel Barrois,[3] Anne-Paule Gimenez-Roqueplo,[4] Michel Leporrier,[5] Nicole Casadevall,[6] Olivier Hermine,[7] Jean-Jacques Kiladjian,[8] André Baruchel,[9] Fadi Fakhoury,[10] Brigitte Bressac-de Paillerets,[3,11] Jean Feunteun,[12] Nathalie Mazure,[13] Jacques Pouysségur,[13] Roland H. Wenger,[2] Stéphane Richard,[1,14] and Betty Gardie[1]

[1]Génétique Oncologique EPHE, INSERM U753, Institut de Cancérologie Gustave Roussy, Villejuif et Faculté de Médecine Paris-Sud, Le Kremlin-Bicêtre, France; [2]Institute of Physiology and Zürich Center for Integrative Human Physiology ZIHP, University of Zürich, Zürich, Switzerland; [3]Service de Génétique, Institut de Cancérologie Gustave Roussy, Villejuif, France; [4]Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Service de Génétique, Paris, France; INSERM, UMR970, Paris-Cardiovascular Research Center at HEGP, Paris, France; Université Paris Descartes, Faculté de Médecine, Paris, France; [5]CHU de Caen, Service d'Hématologie Clinique, France; [6]Hôpital Saint Antoine, Assistance Publique–Hôpitaux de Paris and Pierre et Marie Curie University, Institut Gustave Roussy, Inserm, UMR790, Villejuif, France; [7]Service d'Hématologie, Hôpital Necker-Enfants Malades, AP-HP, Paris, France; [8]Centre d'Investigations Cliniques, Hôpital Saint-Louis, AP-HP, Paris, France; [9]Service d'Hématologie, Hôpital St. Louis, Paris, France; [10]Service de Néphrologie, Hôpital Necker, Paris, France; [11]Unité INSERM U946, Variabilité Génétique et Maladies Humaines, Fondation Jean Dausset/CEPH Unité, Paris, France; [12]Institut de Cancérologie Gustave Roussy, CNRS-UMR8200, Villejuif, France; [13]Institut de Biologie du Développement et Cancer, Université de Nice - Sophia Antipolis, CNRS UMR-6543, France, and [14]Centre Expert National Cancers Rares INCa "PREDIR" and Réseau National INCa, AP-HP, Service d'Urologie, CHU, Le Kremlin-Bicêtre and Service de Néphrologie, Hôpital Necker, Paris, France

Citation: Ladroue C, Hoogewijs D, Gad S, Carcenac R, Storti F, Barrois M, Gimenez-Roqueplo A-P, Leporrier M, Casadevall N, Hermine O, Kiladjian J-J, Baruchel A, Fakhoury F, Bressac-de Paillerets B, Feunteun J, Mazure N, Pouysségur J, Wenger RH, Richard S, and Gardie B. Distinct deregulation of the hypoxia inducible factor by PHD2 *mutants identified in germline DNA of patients with polycythemia. Haematologica 2012;97(1):9-14. doi:10.3324/haematol.2011.044644*

Online Supplementary Figure S1. **Multiple sequence alignment of PHD2 homologs. The alignment starts from amino acid position 151 in human PHD2. Vertebrate homologs across 46 species were extracted using the MULTIZ whole-genome multiple alignment algorithm[1] implemented in the UCSC Genome Browser.[2] Invertebrate homologs were obtained using the FlyBase implemented InParanoid algorithm[3] and a selection of bacterial sequences were added. Species with large gaps were manually omitted. Subsequently, all sequences were realigned using the MAFFT multiple alignment tool with an iterative refinement option incorporating local pairwise alignment information.[4] Gaps of more than three positions introduced in vertebrate PHD2 homologs by alignment to distantly related invertebrate and bacterial sequences are labelled with " | " above the alignment.**



References

1. Blanchette M, Kent WJ, Riemer C, Elnitski L, Smit AF, Roskin KM, et al. Aligning multiple genomic sequences with the threaded blockset aligner. Genome Res. 2004;14(4):708-15.
2. Rhead B, Karolchik D, Kuhn RM, Hinrichs AS, Zweig AS, Fujita PA, et al. The UCSC Genome Browser database: update 2010. Nucleic Acids Res. 2010;38(Database issue):D613-9.
3. Ostlund G, Schmitt T, Forslund K, Kostler T, Messina DN, Roopra S, et al. InParanoid 7: new algorithms and tools for eukaryotic orthology analysis. Nucleic Acids Res. 2010;38(Database issue):D196-203.
4. Katoh K, Kuma K, Toh H, Miyata T. MAFFT version 5: improvement in accuracy of multiple sequence alignment. Nucleic Acids Res. 2005;33(2):511-8.