

Position: CNRS Research Director (DR2)

Education: Ph. D, University Joseph Fourier Grenoble 1991

Location: Plant Physiology and Cellular Laboratory/iRTSV/CEA Grenoble, France

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Research overview: My research interests focus on the structure-function relationships of proteins to understand biological mechanisms at a molecular level. With this aim, I have developed biochemical and structural approaches initially on reaction and mechanism of inhibition of enzymes involved in the synthesis of plant essential amino acids and vitamins, then on mechanism of control of allosteric enzymes and more recently on transcription factors involved in floral development.

Selected publications:

-Curien, G.^{*}, Bastien, O., Robert-Genthon, M., Cornish-Bowden, A., Cardenas, M.L. & Dumas, R. (2009) Understanding regulation of aspartate metabolism with a model based on measured kinetic parameters. **Molecular System Biology**, 5:271.

-Mas-Droux, C., Curien, G., Robert-Genthon, M., Laurencin, M., Ferrer, J.-L.^{*} & Dumas, R.^{*} (2006) A novel organization of ACT domains in allosteric enzymes revealed by the crystal structure of Arabidopsis aspartate kinase. **The Plant Cell**, 18, 1681-1692.

-Mas-Droux, C., Biou^{*}, V. & Dumas, R.^{*} (2006) Allosteric threonine synthase: reorganization of the PLP site upon asymmetric activation through SAM binding to a novel site. **Journal of Biological Chemistry**, 281, 5188-5196.

-Dumas, R.^{*}, Biou, V., Halgand, F., Douce, R. & Duggleby, R. (2001) Enzymology, structure and dynamics of acetohydroxy acid isomeroreductase. **Accounts of Chemical Research**, 34, 399-408.

-Biou, V.^{*}, Dumas, R.^{*}, Cohen-Addad, C., Douce, R., Job, D. & Pebay-Peyroula, E. (1997) The Crystal structure of plant acetohydroxyacid isomeroreductase complexed with NADPH, two magnesium ions and a herbicidal transition state analog determined at 1.65 Å resolution. **The EMBO Journal**, 16, 3405-3415.

Awards:

-Bronze Medal CNRS 1997.

-Mongolfier Price 1996.

Direction or co-direction of Ph. D students:

Gilles Curien, Peter Wessel, Corine Mas-Droux, Djeneb Camara and Camille Sayou.

Complete list of publications:

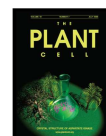
<http://www.researcherid.com/rid/E-1835-2011>

Understanding the molecular function of transcription factors involved in floral development with a focus on leafy:

Coming soon...

Understanding the mechanism of control of allosteric enzymes with a focus on threonine synthase and enzymes containing an ACT domain:

- 1- Dumas, R.*, Cobessi, D., Robin, A.Y., Ferrer, J.-L. & Curien, G. (2012). The many faces of aspartate kinase. **Archives of Biochemistry and Biophysics**, 519, 186-193. (Invited review, Special issue on Allosteric Regulation).
- 2- Robin, A. Y., Cobessi, D., Curien, G., Robert-Genthon, M., Ferrer, J.-L. * and Dumas, R. * (2010). New mode of dimerization of allosteric enzymes with ACT domains revealed by the crystal structure of the aspartate kinase from Cyanobacteria. **Journal of Molecular Biology**, 399, 283-293.
- 3- Curien, G. *, Bastien, O., Robert-Genthon, M., Cornish-Bowden, A., Cardenas, M.L. and Dumas, R. (2009) Understanding regulation of aspartate metabolism with a model based on measured kinetic parameters. **Molecular System Biology**, 5, 271. Recommended F1000.
- 4- Dumas, R. (2008) Plant structural biology. **Plant Physiology and Biochemistry**, 2008, 46, 227. (Guest editor, Special issue on Plant structural biology).
- 5- Curien, G., Biou, V., Mas-Droux, C., Robert - Genthon, M., Ferrer, J.L. and Dumas, R. * (2008) Amino acid biosynthesis: new architectures in allosteric enzymes. **Plant Physiology and Biochemistry**, 46, 325-339. (Special issue on Plant structural biology).
- 6- Curien, G. *, Laurencin, M., Robert-Genthon, M. & Dumas, R. (2007) Allosteric monofunctional aspartate kinase from Arabidopsis. **European Journal of Biochemistry**, 274, 164-176.
- 7- Mas-Droux, C., Biou, V. * & Dumas, R. * (2006) Allosteric threonine synthase: reorganization of the PLP site upon asymmetric activation through SAM binding to a novel site. **Journal of Biological Chemistry**, 281, 5188-5196.
- 8- Mas-Droux, C., Curien, G., Robert-Genthon, M., Laurencin, M., Ferrer, J.-L. * & Dumas, R. * (2006) A novel organization of ACT domains in allosteric enzymes revealed by the crystal structure of Arabidopsis aspartate kinase. **The Plant Cell**, 18, 1681-1692.
- 9- Curien, G. *, Ravel, S., Robert, M. & Dumas, R. (2005) Identification of six novel allosteric effectors of *Arabidopsis thaliana* aspartate kinase-Homoserine dehydrogenase isoforms. Physiological context sets the specificity. **Journal of Biological Chemistry**, 280, 41178-41183.
- 10- Paris, S., Viemon, C., Curien, G. & Dumas, R. * (2003) Mechanism of control of *Arabidopsis thaliana* aspartate kinase-homoserine dehydrogenase by threonine. **Journal of Biological Chemistry**, 278, 5361-5366.



- 11- Curien, G.^{*}, Ravanel, S. & Dumas, R. (2003) Phosphohomoserine branch-point in plant: a numerical and *in vitro* model of the kinetic competition between Arabidopsis cystathionine γ -synthase and threonine synthase. **European Journal of Biochemistry**, 270, 4615-4627.
- 12- Paris, S., Wessel, P. M. & Dumas, R.^{*} (2002) Overproduction, purification and characterization of recombinant bifunctional threonine-sensitive aspartate kinase/homoserine dehydrogenase from *Arabidopsis thaliana*. **Protein Expression and Purification**, 24, 105-110.
- 13- Halgand, F.^{*}, Wessel, P., Laprévote, O. & Dumas R.^{*} (2002) Biochemical and mass spectrometric evidence for quaternary structure modifications of plant threonine deaminase induced by isoleucine. **Biochemistry**, 41, 13767-13773.
- 14- Thomazeau, K., Curien, G., Dumas, R.^{*} & Biou, V.^{*} (2001) Structure of *Arabidopsis thaliana* threonine synthase. **Protein Science**, 10, 638-648.
- 15- Thomazeau, K., Curien, G., Thompson, A., Dumas, R. & Biou, V.^{*} (2001) MAD on threonine synthase : the phasing power of oxidised selenomethionine. **Acta Crystallographica D**, 57, 1137-1340.
- 16- Wessel, P. M., Graciet, E., Douce, R. & Dumas, R.^{*} (2000) Evidence for two distinct effector-binding sites in threonine deaminase by site-directed mutagenesis, kinetic and binding experiments. **Biochemistry**, 39, 15136-15143.
- 17- Curien, G.^{*}, Job, D., Douce, R. & Dumas, R. (1998) Allosteric activation of *Arabidopsis* threonine synthase by S-adenosylmethionine. **Biochemistry**, 37, 13212-13221.
- 18- Curien, G., Dumas, R.^{*}, Ravanel, S. & Douce R. (1996) Characterization of an *Arabidopsis thaliana* cDNA encoding an S-Adenosylmethionine-sensitive threonine synthase. **FEBS letters**, 390, 85-90.

Understanding the reaction and mechanisms of inhibition of enzymes with a focus on key enzymes involved in the synthesis of essentials amino acids and vitamins:

- 19- Raspail, C., Graindorge, M., Moreau, Y., Crouzy, S., Lefebvre, B., Robin, A.Y., Dumas, R. & Matringe, M.^{*} (2011) 4-hydroxyphenylpyruvate dioxygenase catalysis: Identification of catalytic residues and production of a hydroxylated intermediate shared with a structurally unrelated enzyme. **Journal of Biological Chemistry**, 286, 26061-26070.
- 20- Camara, D., Richefeu-Contesto, C., Gambonnet, B., Dumas, R. & Rébeillé, F.^{*} (2011) The synthesis of pABA: Coupling between the glutamine amidotransferase and aminodeoxychorismate synthase domains of the bifunctional aminodeoxychorismate synthase from *Arabidopsis thaliana*. **Archives of Biochemistry and Biophysics**, 505, 83-90.
- 21- Legrand, P., Dumas, R., Seux, M., Rippert, P., Ravelli, R., Ferrer, J.-L.^{*} & Matringe M.^{*} (2006) Biochemical characterization and crystal structure of Synechocystis arogonate dehydrogenase provide insight into catalytic reaction. **Structure**, 14, 767-776.
- 22- Ferrer, J.-L.^{*}, Ravanel, S. Robert, M., & Dumas, R.^{*} (2004) Crystal structures of cobalamin-independent methionine synthase complexed with Zinc, homocysteine and methyltetrahydrofolate. **Journal of Biological Chemistry**, 279, 44235-44238 (Paper of the week).
- 23- Paris, S., Wessel, P. M. & Dumas, R.^{*} (2002) Overproduction, purification and characterization of recombinant aspartate semialdehyde dehydrogenase from *Arabidopsis thaliana*. **Protein Expression and Purification**, 24, 99-104.
- 24- Dumas, R.^{*}, Biou, V., Halgand, F., Douce, R. & Duggleby, R. (2001) Enzymology, structure and dynamics of acetohydroxy acid isomeroreductase. **Accounts of Chemical Research**, 34, 399-408. (Invited review).
- 25- Thomazeau, K., Dumas, R., Halgand, F., Forest, E., Douce, R. & Biou, V.^{*} (2000) Structure of spinach acetohydroxy acid isomeroreductase complexed with its reaction product dihydroxymethylvalerate, manganese and (phospho)-ADP-ribose. **Acta Crystallographica D**, 56, 389-397.

- 26- Proust-De Martin F., Dumas, R. & Field M. J. * (2000) A hybrid-potential free-energy study of the isomerization step of the acetohydroxy acid isomeroreductase reaction. **Journal of American Chemical Society**, 122, 7688-7697.
- 27- Lapr v te, O. *, Serani, L., Das, B.C., Halgand, F., Forest, E. & Dumas, R. (1999) Stepwise building of a 115 kilodaltons macromolecular edifice monitored by electrospray mass spectrometry : the case of acetohydroxy acid isomeroreductase **European Journal of Biochemistry**, 259, 356-359.
- 28- Halgand, H., Dumas, R. *, Biou, V., Andrieu, J.-P., Thomazeau, K., Gagnon, J., Douce, R. & Forest, E. * (1999) Characterization of the conformational changes of acetohydroxy acid isomeroreductase induced by the binding of NADPH, Mg ions and a competitive inhibitor. **Biochemistry**, 38, 6025-6034.
- 29- Wessel, P. M., Biou, V., Douce, R. & Dumas R. * (1998) A loop deletion in the plant acetohydroxy acid isomeroreductase generates active monomer with reduced stability and altered magnesium affinity. **Biochemistry**, 37, 12753-12760.
- 30- Halgand, F., Vives, F., Dumas, R. *, Biou, V., Andersen, J., Andrieu, J.-P., Cantegril, R., Gagnon, J., Douce, R., Forest, E. & Job, D. (1998) Kinetic and mass spectrometric analyses of the interactions between plant acetohydroxy acid isomeroreductase and thiadiazole derivatives. **Biochemistry**, 37, 4773-4781.
- 31- Biou, V. *, Dumas, R. *, Cohen-Addad, C., Douce, R., Job, D. & Pebay-Peyroula, E. (1997) The Crystal structure of plant acetohydroxy acid isomeroreductase complexed with NADPH, two magnesium ions and a herbicidal transition state analog determined at 1.65   resolution. **The EMBO Journal**, 16, 3405-3415.
- 32- Dumas, R. *, Biou, V. & Douce, R. (1997) Purification and characterization of a fusion protein of plant acetohydroxy acid synthase and acetohydroxy acid isomeroreductase. **FEBS letters**, 408, 156-160.
- 33- Dumas, R. *, Butikofer, M.-C., Job, D. & Douce, R. (1995) Evidence for two catalytically different magnesium binding sites in acetohydroxy acid isomeroreductase by site-directed mutagenesis. **Biochemistry**, 34, 6026-6036.
- 34- Dumas, R., Job, D., Douce, R., Pebay-Peyroula, E. & Cohen-Addad, C. (1994) Crystallization and preliminary crystallographic data for acetohydroxy acid isomeroreductase from *Spinacia oleracea*. **Journal of Molecular Biology**, 242, 578-581.
- 35- Dumas, R. *, Cornillon-Bertrand, C., Guigue-Talet, P., Genix, P., Douce, R. & Job, D. (1994) Interactions of plant acetohydroxy acid isomeroreductase with reaction intermediate analogues. Correlation of the slow, competitive, inhibition kinetics of enzyme activity and herbicidal effects. **Biochemical Journal**, 301, 813-820.
- 36- Dumas, R. *, Curien, G., De Rose, R. & Douce, R. (1993) Branched chain amino acids biosynthesis in plants: molecular cloning and characterization of the gene encoding acetohydroxy acid isomeroreductase from *Arabidopsis thaliana*. **Biochemical Journal**, 294, 821-828.
- 37- Curien, G., Dumas, R. * & Douce R. (1993) Nucleotide sequence and characterization of a cDNA encoding the acetohydroxy acid isomeroreductase from *Arabidopsis thaliana*. **Plant Molecular Biology**, 21, 717-722.
- 38- Dumas, R., Job, D., Ortholand, J.-Y., Emeric, G., Greiner, A. & Douce, R. * (1992) Isolation and kinetic properties of acetohydroxy acid reductoisomerase from spinach chloroplasts overexpressed in *Escherichia coli*. **Biochemical Journal** 288, 865-874.
- 39- Dumas, R., Lebrun M. & Douce, R. * (1991) Isolation, characterization and sequence analysis of a full-length cDNA clone encoding acetohydroxy acid reductoisomerase from spinach chloroplasts. **Biochemical Journal** 277, 69-75.
- 40- Dumas, R., Joyard, J. & Douce, R. * (1989) Purification and characterization of acetohydroxy acid isomeroreductase from spinach chloroplasts. **Biochemical Journal** 262, 971-976.

Miscellaneous:

- 41- Dumas, R., Joyard, J. & Douce, R. * (1989) Effect of sulphate on glutamate synthesis by intact spinach (*Spinacia oleracea*) chloroplasts. **Biochemical Journal** 259, 769-774.
- 42- Pascal, N.*, Dumas, R. & Douce, R. (1990) Comparison of the kinetic behaviour toward pyridine nucleotides of NADP-linked dehydrogenases from plant mitochondria. **Plant Physiology** 94, 189-193.

Patents:

- 43- Dumas, R., Lebrun, M.-H., Zundel, J.-L., Effantin, G. & Morin, V.: Use of acetohydroxy acid isomeroreductase inhibitors for treating fungal diseases affecting crops. Bayer Cropscience Mar, 14 2003: FR2829363; Jun, 9 2004: EP1424899.
- 44- Matringe, M., Rippert, P., Dubald, M. & Dumas, R.: Transformed plants with enhanced prenylquinone biosynthesis. Bayer Cropscience Mar, 12 2004: FR2844142; May 2005: KR 1020057004192; Jun, 8 2005: EP1537216 ; Oct, 26 2005: CN 03824326.

