

# AMPK, more than just a metabolic sensor in cardiac pathologies



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The AMP-activated protein kinase (AMPK) has been firstly discovered to be activated under metabolic stress conditions such as myocardial ischemia. Its protective action during an ischemic episode has been demonstrated by several research groups. By targeting metabolism, AMPK helps the heart to survive under such deleterious conditions. However, AMPK action extends beyond metabolism and acute stress conditions. Indeed, it has been more recently shown that AMPK acts as protector of the heart in several chronic diseases such heart failure, diabetic cardiomyopathy and cardiac hypertrophy by acting in cardiomyocytes but also on the other cell types such as fibroblasts. Very recently, our group discovered a connection between AMPK and a particular post-translational modification called O-GlcNAcylation, this interplay acting a major role in the development of cardiac hypertrophy. The lecture will focus on the different protective roles of cardiac AMPK, particularly focusing on the more recent advances linking AMPK and OGlcNAcylation.

## **Selected references:**

1. Gélinas R. et al., AMPK activation counteracts cardiac hypertrophy by reducing OGlcNAcylation (2018) *Nat. Comm.*, 9, 374.
2. Gélinas R. et al., AMP-activated protein kinase and O-GlcNAcylation, two partners tightly connected to regulate key cellular processes (2018) *Front. Endocrinol.*, 9, 519.
3. Mailleux F. et al., O-GlcNAcylation, enemy or ally during cardiac hypertrophy development? (2016) *Biochim. Biophys. Acta*, 1862, 2232-2243.
4. Horman S. et al., AMP-activated protein kinase in the control of cardiac metabolism and remodeling (2012) *Curr. Heart Fail. Rep.*, 9, 164-173.

## **Most relevant Publications:**

### **2018**

92. Gélinas R., Dontaine J., Horman S., Beauloye C., Bultot L. and Bertrand L. AMP-activated protein kinase and O-GlcNAcylation, two partners tightly connected to regulate key cellular processes (2018) *Front. Endocrinol.*, 9, 519 (IF: 3.5, CI: -)
90. Renguet E., Bultot L., Beauloye C., Horman S. and Bertrand L. The regulation of insulinstimulated cardiac glucose transport via protein acetylation (2018) *Front. Cardiovasc. Med.*, 5, 70 (IF:-, CI:-)
89. Gélinas R., Mailleux F., Dontaine J., Bultot L., Demeulder B., Ginion A., Daskalopoulos E.P., Esfahani H., Dubois-Deruy E., Lauzier B., Gauthier C., Olson A.K., Bouchard B., DesRosiers C., Viollet B., Sakamoto K, Balligand J.L., Vanoverschelde J.L., Beauloye C., Horman S. and Bertrand L. AMPK activation couteracts cardiac hypertrophy by reducing OglcNAcylation (2018) *Nat. Comm.*, 9, 374 (IF: 13.0, CI: -)

### **2017**

86. Renguet E., Ginion A., Gélinas R., Bultot L., Auquier J., Robillard Frayne I., Daneault C., Vanoverschelde J.-L., Des Rosiers C., Hue L., Horman S., Beauloye C. and Bertrand L. Metabolism and acetylation contribute to leucine-mediated inhibition of cardiac glucose uptake (2017) *Am. J. Physiol. Heart Circ. Physiol.*, 313, H432-H445. (IF: 3.8,CI: 1)

### **2016**

84. Mailleux F., Gélinas R., Beauloye C., Horman S. and Bertrand L. O-GlcNAcylation, enemy or ally during cardiac hypertrophy development? (2016) *Biochim. Biophys. Acta*, 1862, 2232-2243. (IF: 5.2, CI: 6)

80. Dascalopoulos E.P., Dufey C., Bertrand L., Beauloye C. and Hormann S. AMPK in cardiac fibrosis and repair: Actions beyond metabolic regulation (2016) *J. Mol. Cell. Cardiol.*, 91, 188-200. (IF: 5.1, CI: 25)

## 2015

78. Beauloye C., Hormann S. and Bertrand L. Even is better than odd: One fat may conceal another (2015) *Am. J. Physiol. Heart Circ. Physiol.*, 309, H1112-H1114. (IF: 4.0, CI: 1)

## 2014

76. Foretz M., Guigas B., Bertrand L., Pollak M. and Viollet B. Metformin: from mechanism of action to therapies (2014) *Cell Metab.*, 20, 953-966. (IF: 16.7, CI: 247)

73. Timmermans A.D., Balteau M., Gélinas R., Renguet E., Ginion A., de Meester C., Sakamoto K., Balligand J.L., Bontemps F., Vanoverschelde J.L., Hormann S., Beauloye C. and Bertrand L. A-769662 potentiates the effect of other AMP-activated protein kinase activators on cardiac glucose uptake (2014) *Am. J. Physiol. Heart Circ. Physiol.*, 306, H1619-1630. (IF: 4.0, CI: 21)

68. de Meester C., Timmermans A.D., Balteau M., Ginion A., Roelants V., Noppe G., Porporato P.E., Sonveaux P., Viollet B., Sakamoto K., Feron O., Hormann S., Vanoverschelde J.L., Beauloye C. and Bertrand L. Role of AMP-activated protein kinase in regulating hypoxic survival and proliferation of mesenchymal stem cells (2014) *Cardiovasc. Res.*, 101, 20-29. (IF: 5.9, CI: 21)

## 2013

64. Demeulder B., Zarrinpasheh E., Ginion A., Viollet B., Hue L., Rider M.H., Vanoverschelde JL., Beauloye C., Hormann S. and Bertrand L. Differential regulation of eEF2 and p70S6K by AMPKalpha2 in heart (2013) *Biochim. Biophys. Acta.*, 1832, 780-790. (IF: 5.4, CI: 10)

## 2012

62. Hormann S., Beauloye C., Vanoverschelde J.L. and Bertrand L. AMP-activated protein kinase in the control of cardiac metabolism and remodeling (2012) *Curr. Heart Fail. Rep.*, 9, 164-173. (IF: -, CI: 45)

60. Gruson D., Ginion A., Lause P., Ketelslegers J.M., Thissen J.P. and Bertrand L. Urotensin II and urocortin trigger the expression of myostatin, a negative regulator of cardiac growth, in cardiomyocytes (2012) *Peptides*, 33, 351-353. (IF: 2.7, CI: 16)

## **2011**

57. Beauloye C., Bertrand L., Horman S. and Hue L. AMPK, a potential therapeutic target against the transition from cardiac injury to heart failure (2011) *Cardiovasc. Res.*, 90, 224-233. (IF: 6.1, CI: 128)
53. Ginion A., Auquier J., Benton CR., Mouton C., Vanoverschelde JL., Hue L., Horman S., Beauloye C. and Bertrand L. Inhibition of the mTOR/p70S6K pathway is not involved in the insulin-sensitizing effect of AMPK on cardiac glucose uptake (2011) *Am. J. Physiol. Heart Circ. Physiol.*, 301, H469-H477. (IF: 3.9, CI: 40)

## **2010**

50. Sanchez Canedo C., Demeulder B., Ginion A., Bayascas JR., Balligand JL., Alessi DR., Vanoverschelde JL., Beauloye C., Hue L. and Bertrand L. Activation of the cardiac mTOR/p70S6K pathway by leucine requires PDK1 and correlates with PRAS40 phosphorylation (2010) *Am. J. Physiol. Endocrinol. Metab.*, 298, E761-E769. (IF: 4.7, CI: 46)

## **2009**

49. Viollet B, Athea Y., Mounier R., Guigas B., Zarrinpassneh E., Horman S., Devin-Leclerc J., Beauloye C., Foretz M., Andreelli F., Ventura-Clapier R. and Bertrand L. AMPK : Lessons from animal models (2009) *Front. Biosci.*, 14, 19-44. (IF: 3.3, CI: 232)

## **2008**

44. Bertrand L., Horman S., Beauloye C. and Vanoverschelde J.L. Insulin signalling in the heart (2008) *Cardiovasc. Res.*, 79, 238-248. (IF: 5.9, CI: 198)
42. Zarrinpassneh E., Beauloye C., Ginion A., Pouleur A.C., Havaux X., Hue L., Viollet B., Vanoverschelde J.L. and Bertrand L. AMPKa2 counteracts the development of cardiac hypertrophy induced by isoproterenol (2008) *Biochem. Biophys. Res. Com.*, 376, 677-681. (IF: 2.8, CI: 40)