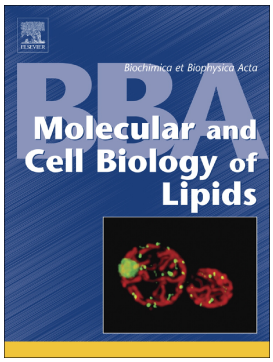
Accepted Manuscript



Identification of lipases with activity towards monoacylglycerol by criterion of conserved cap architectures

Lina Riegler-Berket, Andrea Leitmeier, Philipp Aschauer, Ingrid Dreveny, Monika Oberer

PII: S1388-1981(18)30050-7
DOI: doi:10.1016/j.bbalip.2018.03.009
Reference: BBAMCB 58265

To appear in:

Received date: 3 November 2017
Revised date: 9 March 2018
Accepted date: 27 March 2018

Please cite this article as: Lina Riegler-Berket, Andrea Leitmeier, Philipp Aschauer, Ingrid Dreveny, Monika Oberer , Identification of lipases with activity towards monoacylglycerol by criterion of conserved cap architectures. The address for the corresponding author was captured as affiliation for all authors. Please check if appropriate. Bbamcb(2018), doi:10.1016/j.bbalip.2018.03.009

Identification of lipases with activity towards monoacylglycerol by criterion of conserved cap architectures

Lina Riegler-Berket[1,2], Andrea Leitmeier[1,2], Philipp Aschauer[1,2], Ingrid Dreveny[3] and Monika Oberer[1,2*]

1) Institute of Molecular Biosciences, University of Graz; Austria
2) BioTechMed-Graz, Austria
3) School of Pharmacy, University of Nottingham, University Park, Nottingham, NG7 2RD, UK

* to whom correspondence should be addressed

Abstract:

Monoacylglycerol lipases (MGL) are a subclass of lipases that predominantly hydrolyze monoacylglycerol into glycerol and free fatty acid. MGLs are ubiquitous enzymes across species and play a role in lipid metabolism, affecting energy homeostasis and signaling processes. Structurally, MGLs belong to the α/β hydrolase fold family with a cap covering the substrate binding pocket. Analysis of the known 3D structures of human, yeast and bacterial MGLs revealed striking similarity of the cap architecture. Since MGLs from different organisms share very low sequence similarity, it is difficult to identify MGLs based on the amino acid sequence alone. Here, we investigated whether the cap architecture could be a characteristic feature of this subclass of lipases with activity towards MG and whether it is possible to identify MGLs based on the cap shape. Through database searches, we identified the structures of five different candidate α/β hydrolase fold proteins with unknown or reported esterase activity. These proteins exhibit cap architecture similarities to known human, yeast and bacterial MGL structures. Out of these candidates we confirmed MGL activity for the protein LipS, which displayed the highest structural similarity to known MGLs. Two further enzymes, Avi_0199 and VC1974, displayed low level MGL activities. These findings corroborate our hypothesis that this conserved cap architecture can be used as criterion to identify lipases with activity towards MGs.

Keywords: Monoacylglycerol lipase, monoglyceride lipase, lipase cap, conserved cap architecture, lipase lid, enzyme kinetics

1. Introduction

Monoacylglycerol lipases (MGLs) are hydrolytic enzymes found in all domains of life. As their physiological role, MGLs metabolize lipid intermediates involved in energy homeostasis by producing fatty acids for energy production and in signaling processes (e.g. endocannabinoid signaling) [1–3]. MGLs from human [4–6], rat [7], yeast [8], plant [9] and several bacterial [2,10–12] species have been studied biochemically since the 1960s.

Abbreviations

MGL, monoacylglycerol lipase; ABH, α/β hydrolase; MG, monoacylglycerol; hMGL, monoacylglycerol lipase from *Homo sapiens*; bMGL, monoacylglycerol lipase from *Bacillus species*. H-257