Chapter X
Bacterial β–Barrel Outer Membrane Proteins:
A Common Structural Theme Implicated in a Wide Variety of Functional Roles

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ABSTRACT

β-barrel outer membrane proteins constitute the second and less well-studied class of transmembrane proteins. They are present exclusively in the outer membrane of Gram-negative bacteria and presumably in the outer membrane of mitochondria and chloroplasts. During the last few years, remarkable advances have been made towards an understanding of their functional and structural features. It is now well-known that β-barrels are performing a large variety of biologically important functions for the bacterial cell. Such functions include acting as specific or non-specific channels, receptors for various compounds, enzymes, translocation channels, structural proteins, and adhesion proteins. All these functional roles are of great importance for the survival of the bacterial cell under various environmental conditions or for the pathogenic properties expressed by these organisms. This chapter reviews the currently available literature regarding the structure and function of bacterial outer membrane proteins. We emphasize the functional diversity expressed by a common structural motif such as the β-barrel, and we provide evidence from the current literature for dozens of newly discovered families of transmembrane β-barrels.

INTRODUCTION

Integral membrane proteins are divided into two distinct structural classes, the α-helical membrane proteins and the β-barrel membrane proteins. α-helical membrane proteins class is the more abundant and well studied, since such proteins are located mostly in the cell membranes of both prokaryotic and eukaryotic organisms, performing a variety of biologically important functions. Proteins of this class have their membrane spanning regions forming α-helices consisting mainly of hydrophobic residues (von Heijne 1999). These proteins have been studied extensively in a computational manner during the last few years and a variety of prediction algorithms have been proposed (Möller, Croning et al. 2001). Members of the latter class (β-barrel membrane proteins) are located in the outer membrane of Gram-negative bacteria, and presumably in the outer membrane of chloroplasts and mitochondria, a fact explained by the theory of endosymbiosis. The members of this class are having their membrane spanning segments formed by antiparallel amphipathic β-strands, creating a channel in a form of barrel that spans the outer membrane (Schulz 2002).

A continuously increasing number of β-barrel proteins located in the bacterial outer membrane are characterized, and a number of structures have been solved at atomic resolution (Schulz 2002). These proteins have been shown to perform a wide variety of functions such as active ion transport, passive nutrient uptake, membrane anchoring, adhesion, and catalytic activity. Considering the fact that a large number of pathogens are actually bacteria belonging to the Gram-negative bacteria class and the important biological functions in which outer membrane proteins are involved in, it is not a surprise that these proteins attract an increased medical interest.

In the following sections we will fist try to describe briefly the structural features observed so far in the β-barrel outer membrane proteins with known three dimensional structure. Then, we will discuss the available computational methods used for the prediction of the transmembrane strands of β-barrel outer membrane proteins as well as for the discrimination of such proteins from water-soluble and alpha-helical membrane proteins. Afterwards, we will discuss in detail the functional roles in which β-barrel outer membrane proteins are implicated into. Emphasis will be given in newly characterized families of β-barrel outer membrane proteins that are involved in a series of crucial for the survival of the bacterial cell functions and in the implications for the pathogenicity of these organisms.

STRUCTURAL FEATURES OF β-BARRELS

The β-barrel is a protein fold occurring in soluble proteins as well in transmembrane ones. A β-barrel may be considered as a β-sheet that twists and coils to form a closed barrel-shaped structure, which is stabilized by the hydrogen bonds formed by the sheet edges (first and last strands). The observed so far transmembrane β-barrels preferentially lay their axis along the membrane normal and are exclusively composed of meandering all-next-neighbor antiparallel β-strands, suggesting a repeating β-hairpin structural motif. It has been shown that any type of β-barrel can accurately be described solely by two parameters, namely the number of β-strands n and the shear number S. S is a measure of the stagger of the strands in the sheet. Theoretical analysis combined with available three dimensional structures proved that these two parameters determine all other features of the β-barrel (Murzin, Lesk et al. 1994; Murzin, Lesk et al. 1994). Currently, available high-resolution structures of transmembrane β-barrel proteins include β-barrels of varying features, with $8 \leq n \leq 22$ and $8 \leq S \leq 24$ (Table 1). Furthermore,