Edge strand of Escherichia coli BepA interacts with immature LptD on the β-barrel assembly machine to direct it to on- and off-pathways

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Manuscript Source: https://www.biorxiv.org/content/10.1101/2021.03.28.437416v1

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Research Paper Sections:

The sections of the research paper input text parsed in this audit.

Section No.	Headings	Sentences
Section: 1	Abstract	11
Section: 2	Introduction	16
N/A		0

Edge strand of Escherichia coli BepA interacts with immature LptD on the β-barrel assembly machine to direct it to on- and off-pathways

S1 [001] Abstract

S1 [002] The outer membrane (OM) of gram-negative bacteria is crucial for maintenance of cell viability as it functions as a selective permeability barrier.

The outer membrane ...
... (OM) ...
... of gram-negative bacteria is crucial ...
... for maintenance ...
... of cell viability ...
... as it functions ...
... as a selective permeability barrier.

S1 [003] Escherichia coli periplasmic Zn-metallopeptidase BepA contributes to the maintenance of OM integrity through its involvement in the biogenesis and degradation of an essential OM protein, LptD, a β-barrel component of the lipopolysaccharide translocon.

Escherichia coli periplasmic Zn-metallopeptidase BepA contributes ...

- ... to the maintenance ...
 ... of OM integrity ...
 ... through its involvement ...
 ... in the biogenesis ...
 ... and degradation ...
 ... of an essential OM protein, ...
 ... LptD, ...
 ... a β-barrel component ...
 ... of the lipopolysaccharide translocon.
- **S1 [004]** We have previously shown that BepA either promotes the maturation of LptD when it is on the normal assembly pathway (on-pathway) or degrades it when its assembly is compromised (off-pathway).

We have previously shown ...
... that BepA either promotes the maturation ...
... of LptD ...
... when it is ...
... on the normal assembly pathway ...
... (on-pathway) ...
... or degrades it ...
... when its assembly is compromised ...
... (off-pathway).

S1 [005] BepA performs these functions possibly on the β -barrel assembly machinery (BAM) complex.

```
BepA performs these functions possibly ... ... on the \beta-barrel assembly machinery ... ... (BAM) ... ... complex.
```

S1 [006] However, the mechanistic details of how BepA recognizes and directs the LptD assembly intermediates to different pathways remains unclear.

```
However, ...
... the mechanistic details ...
... of how BepA recognizes ...
... and directs the LptD assembly intermediates ...
... to different pathways remains unclear.
```

S1 [007] Here, we performed site-directed mutagenesis and crosslinking experiments to explore the interactions among BepA, LptD, and the BAM complex.

```
Here, ...
... we performed site-directed mutagenesis ...
... and crosslinking experiments ...
... to explore the interactions ...
... among BepA, ...
... LptD, ...
... and the BAM complex.
```

S1 [008] We found that the interaction of the BepA edge strand located adjacent to the active site with LptD was crucial not only for proteolysis but also for assembly promotion of LptD.

```
We found ...
... that the interaction ...
... of the BepA edge strand located adjacent ...
... to the active site ...
... with LptD was crucial not ...
... only ...
... for proteolysis ...
... but also ...
... for assembly promotion ...
... of LptD.
```

S1 [009] Site-directed crosslinking analysis indicated that the unstructured N-terminal half of the β -barrel-forming domain of an LptD assembly intermediate directly contacts with the BepA edge strand.

```
Site-directed crosslinking analysis indicated ... ... that the unstructured N-terminal half ... ... of the \beta-barrel-forming domain ... ... of an LptD assembly intermediate directly contacts ... ... with the BepA edge strand.
```

S1 [010] Furthermore, the C-terminal region of the β -barrel-forming domain of the BepA-bound LptD intermediate interacted with a "seam" strand of BamA, suggesting that BepA recognized LptD assembling on the BAM complex.

Furthermore, ...

```
... the C-terminal region ...
... of the β-barrel-forming domain ...
... of the BepA-bound LptD intermediate interacted ...
... with a "seam" ...
... strand ...
... of BamA, ...
... suggesting ...
... that BepA recognized LptD assembling ...
... on the BAM complex.
```

S1 [011] Our findings provide important insights into the involvement of BepA in the maintenance of OM structure and function, which can be helpful in developing OM-targeted novel drugs.

Our findings provide important insights ...
... into the involvement ...
... of BepA ...
... in the maintenance ...
... of OM structure ...
... and function, ...
... which can be helpful ...
... in developing OM-targeted novel drugs.

S2 [012] Introduction

S2 [013] The cell envelope of diderm bacteria is composed of two membranes, namely the inner (cytoplasmic) membrane (IM) and the outer membrane (OM).

The cell envelope ...
... of diderm bacteria is composed ...
... of two membranes, ...
... namely the inner ...
... (cytoplasmic) ...
... membrane ...
... (IM) ...
... and the outer membrane ...
... (OM).

S2 [014] The intermembrane space, known as periplasmic space, contains a peptidoglycan layer.

```
The intermembrane space, ...
... known ...
... as periplasmic space, ...
... contains a peptidoglycan layer.
```

S2 [015] The OM is the outermost layer of a cell directly facing the external milieu and acts as a selective permeability barrier that prevents the penetration of toxic compounds including antibiotics (1).

```
The OM is the outermost layer ...
... of a cell directly facing the external milieu ...
```

```
... and acts ...
... as a selective permeability barrier ...
... that prevents the penetration ...
... of toxic compounds including antibiotics ...
... (1).
```

S2 [016] The cell surface localization as well as the functional impotence of the OM make its components suitable drug targets.

```
The cell surface localization ...
... as well ...
... as the functional impotence ...
... of the OM make its components suitable drug targets.
```

S2 [017] Outer membrane proteins (OMPs), generally exhibiting a β-barrel fold formed by more than 8 β-strands, play important roles in maintaining the structural and functional integrity of the OM (2).

```
Outer membrane proteins ...
... (OMPs), ...
... generally exhibiting a β-barrel fold formed ...
... by more than 8 β-strands, ...
... play important roles ...
... in maintaining the structural ...
... and functional integrity ...
... of the OM ...
... (2).
```

S2 [018] Therefore, irregularities in OMP biogenesis result in elevated cellular sensitivity to toxic compounds (3, 4).

```
Therefore, ...
... irregularities ...
... in OMP biogenesis result ...
... in elevated cellular sensitivity ...
... to toxic compounds ...
... (3, 4)...
...
```

S2 [019] After synthesis in the cytoplasm and following translocation across the IM to the periplasm through the SecYEG translocon, OMPs are delivered to the OM by periplasmic chaperones such as DegP, Skp, and SurA, and are finally integrated into the OM (2, 5, 6).

```
After synthesis ...
... in the cytoplasm ...
... and following translocation ...
... across the IM ...
... to the periplasm ...
... through the SecYEG translocon, ...
... OMPs are delivered ...
... to the OM ...
... by periplasmic chaperones ...
... such as DegP, ...
... Skp, ...
```

End of Sample Audit

This is a truncated Manuscript Microscope Sample Audit.

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