STRUCTURAL BASIS OF LIPOPROTEIN SIGNAL PEPTIDASE II ACTION AND INHIBITION BY THE ANTIBIOTIC GLOBOMYCIN

LUTZ VOGELEY,1* TOUFIC EL ARNAOUT,1* JONATHAN BAILEY,1* PHILLIP J. STANSFELD,2
COILIN BOLAND,1 MARTIN CAFFREY1†

陈沫　信息学院　20163171l0022

2016.12.12

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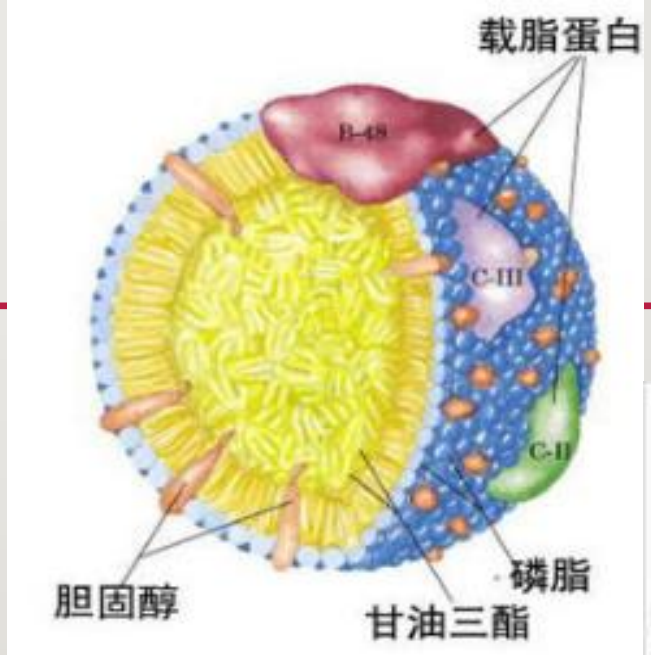
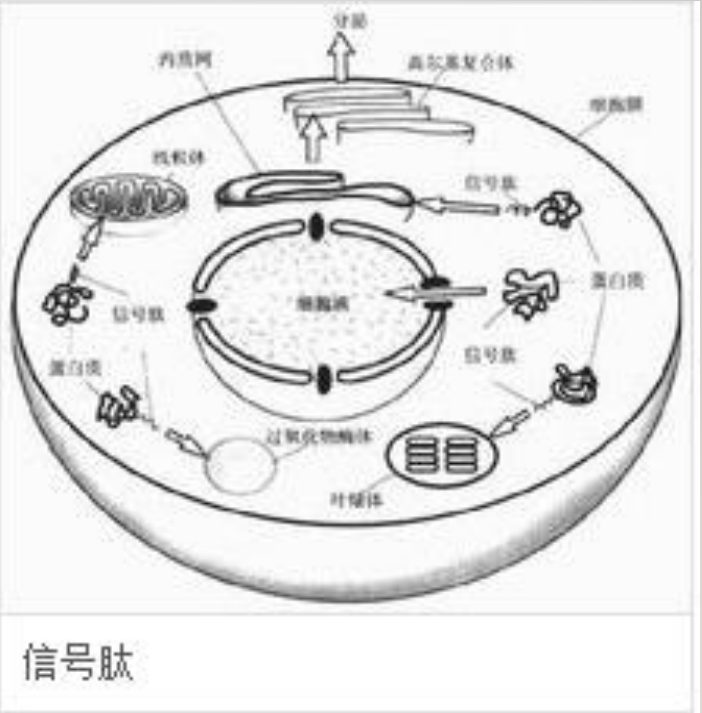
- 方法（methods） & 结果（results）
- 结论（conclusions）
- 总结（summaries）

PART I
BACKGROUND

BACKGROUND

- Lipoproteins
- Globomycin
- Signal peptide
- Signal peptidase





信号肽

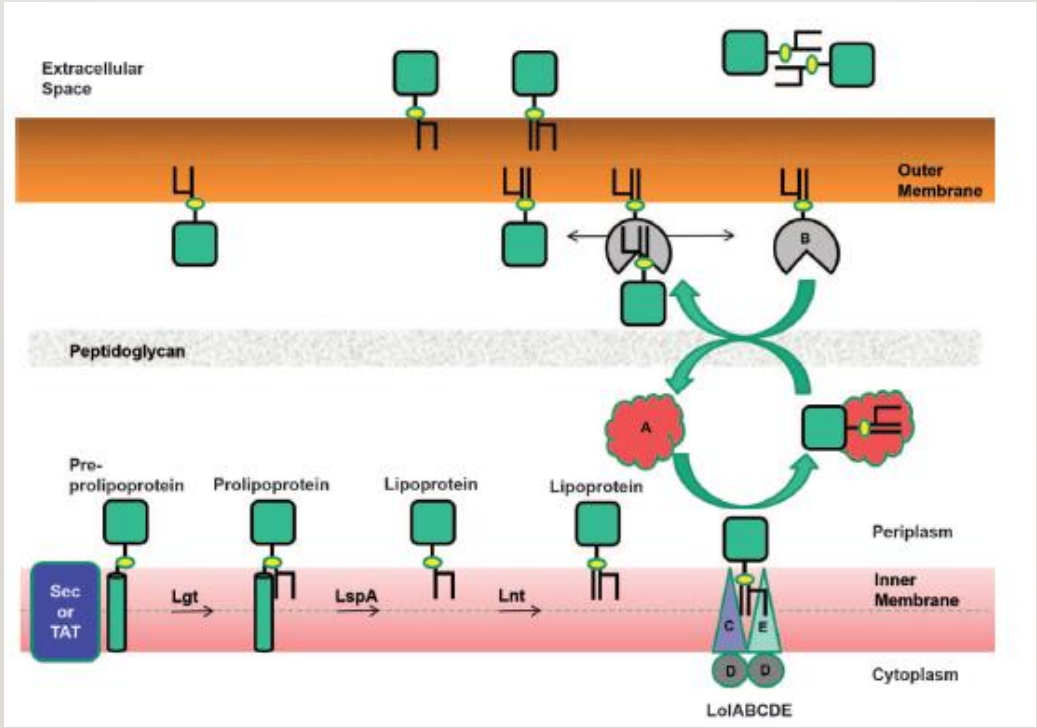
BACKGROUND

- *T*he threat of antibiotic resistance is recognized as a serious public health issue.
- With functions that range from cell envelope structure to signal transduction and transport lipoproteins constitute 2 to 3%of bacterial genomes and play critical roles in bacterial physiology, pathogenicity, and antibiotic resistance.
- LspA, as a key enzyme involved in the posttranslational processing of lipoproteins in Pseudomonas aeruginosa, an opportunistic human pathogen, is a target for antibiotic development

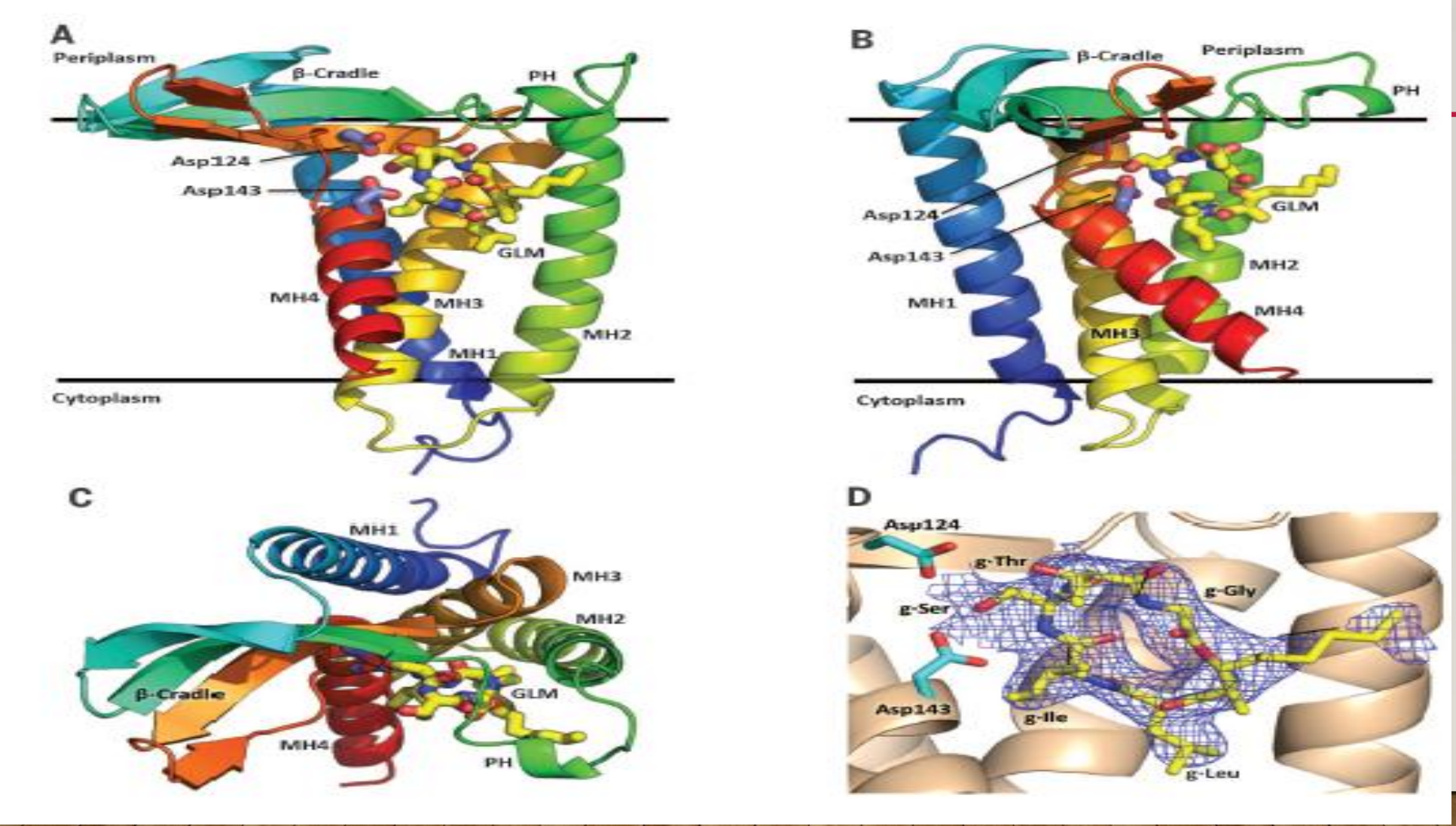
PART II
METHODS & RESULTS

- the crystal structure ——Pseudomonas aeruginosa complexed with the antimicrobial globomycin at 2.8 angstrom resolution
- Crystallization trials————obtain a crystal structure of LspA
- Mutagenesis studies————identify LspA as an aspartyl peptidase
- molecular mimicry————globomycin appears to inhibit by acting as a noncleavable peptide thatsterically blocks the active site.

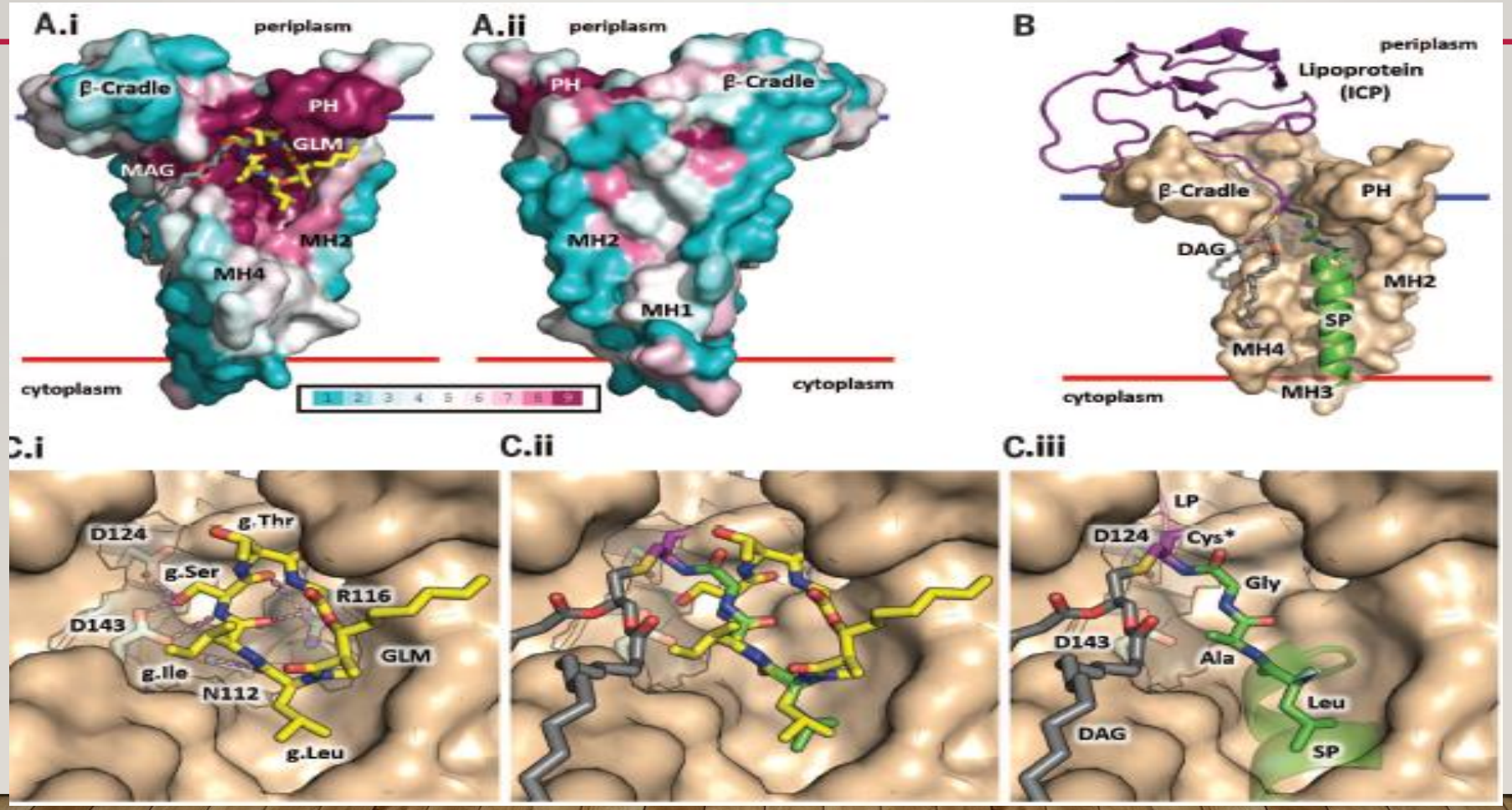
POSTTRANSLATIONAL PROCESSING LEADING TO LIPOPROTEIN MATURATION IN GRAM-NEGATIVE BACTERIA.



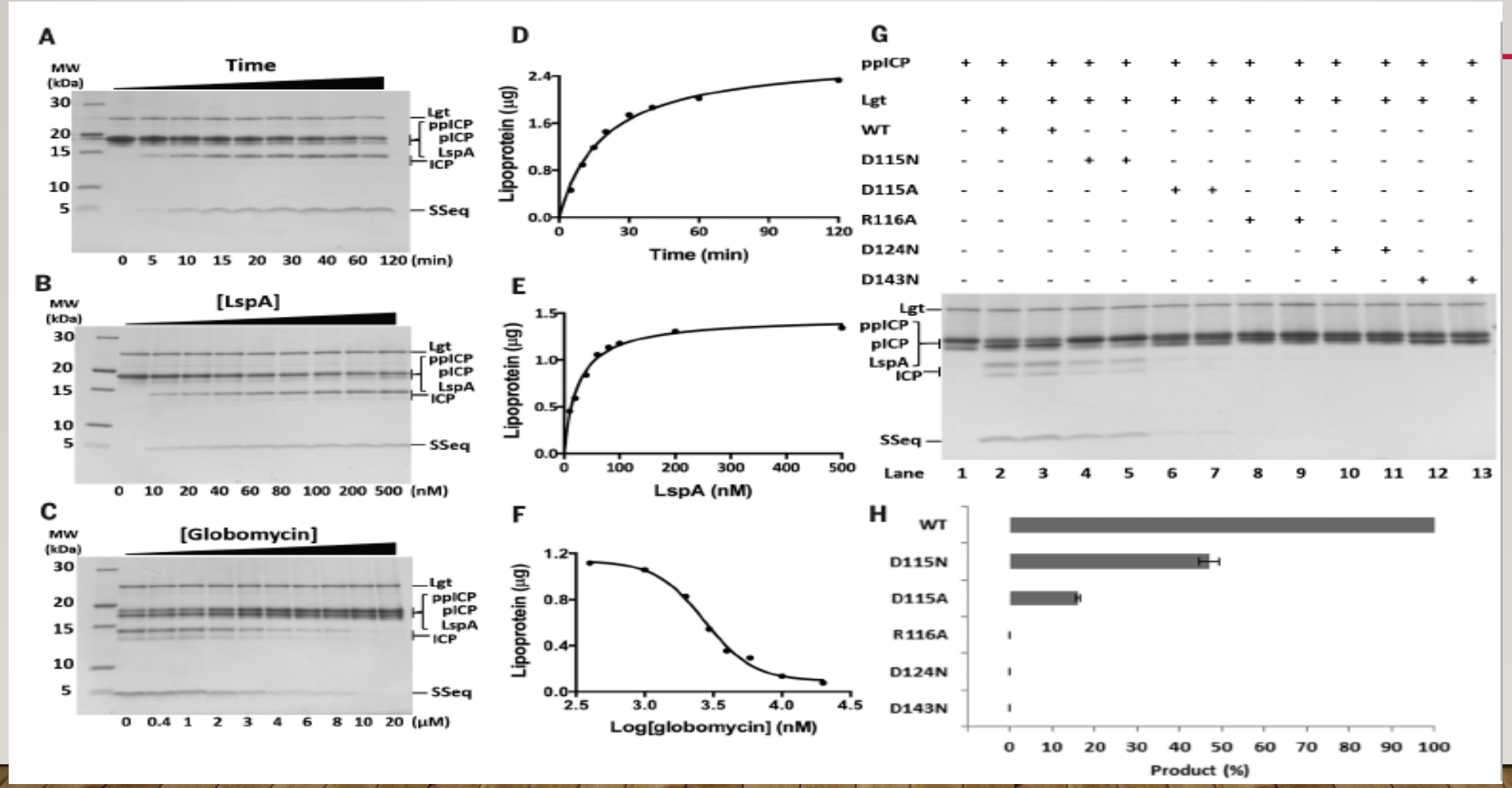
LSPA-GLOBOMYCIN COMPLEX STRUCTURE.



CONSERVED RESIDUES IN ANDGLOBOMYCIN AND PROLIPOPROTEIN BINDING TO LSPA.



ENDOPEPTIDASE ACTIVITY OF LSPA WITH THE SUBSTRATE PROLIPOPROTEIN, GENERATED IN SITU, BASED ON THE PREPROLIPOPROTEIN ICP.



PART III
CONCLUSIONS

CONCLUSION

- LspA is an aspartyl endopeptidase, it is a suitable target with which to explore the thousands of inhibitors developed for other medically relevant aspartyl proteases

- This structure should inform rational antibiotic drug discovery.

PART Ⅳ
SUMMARIES

主要结论：

LSPA 是天冬氨酸肽酶，可作为抗生素发展的靶标，是常规的抗生素类药物发现过程需要了解的结构。

- 启发（设计实验思路，方法）
- 实验设计合理（structure-properties通过探索结构研究性质）
- 实验方法多样（MDS，MM，MS）
- 结果分析清晰（一个实验一个结果，逻辑清晰）

- 改进：
- 实验细节省略过多，不利于别人进行重复。