Exploring the mechanism of Bruceine D against cervical cancer by network pharmacology and the effect of Bruceine D on the EGFR pathway

Jufan Zhu2, Yuanqiu Wang1, Simeng Yang1, Yuli Wang1, Yan Hu1, Xinyue Dai1
1 Department of Gynecology, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China
2 Institute of Organoid Technology, Kunming Medical University, Kunming, China
E-mail: yue10@139.com

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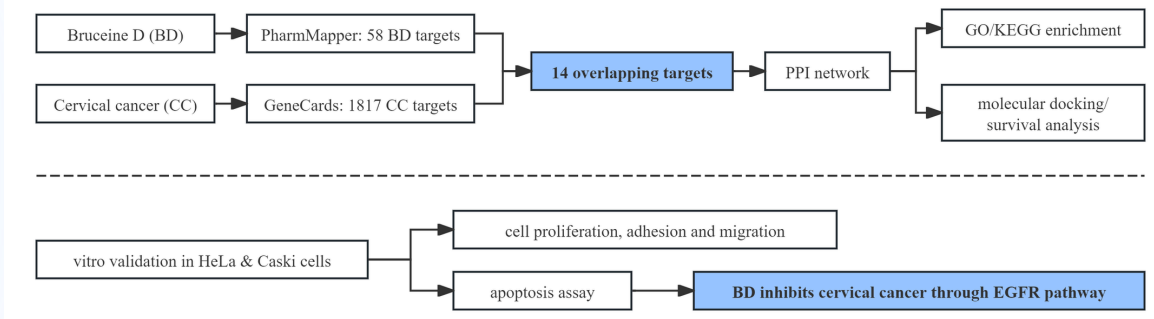
Introduction

- **Cervical cancer** is listed as the **fourth top** malignancy and a chief contributor to cancer deaths amongst women internationally.
- **Bruceine D (BD)**, a prominent active component of Brucea javanica, has been **widely used** in lung cancer, hepatocellular carcinoma, and pancreatic cancer. However, the anticancer effects of **BD on CC remain largely unexplored**, and the underlying mechanisms are still unclear.
- The epidermal growth factor receptor (**EGFR**) is a membrane-spanning glycoprotein. Its **dysregulation and overexpression** contribute to the etiology of diverse malignancies, particularly in cervical cancer.

Methods



Results

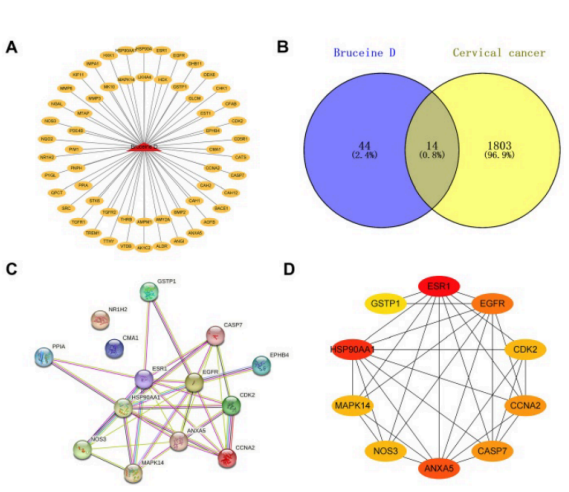


Fig 1. **Network pharmacology** of Bruceine D against cervical cancer.

14 targets

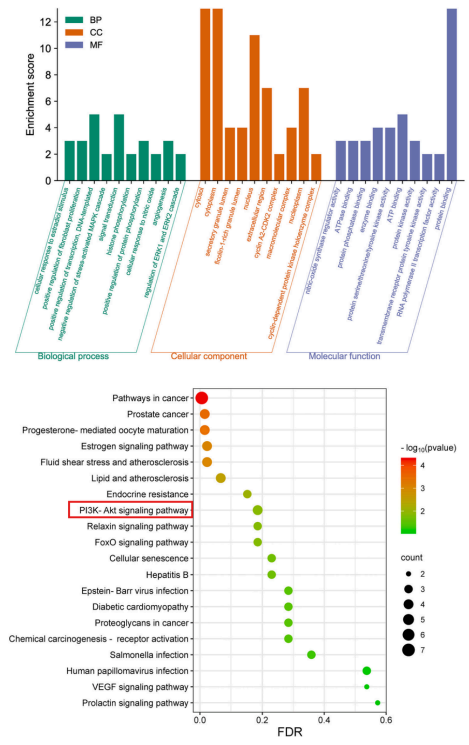


Fig 2. **GO and KEGG** pathway analyses

PI3K/Akt signaling pathway

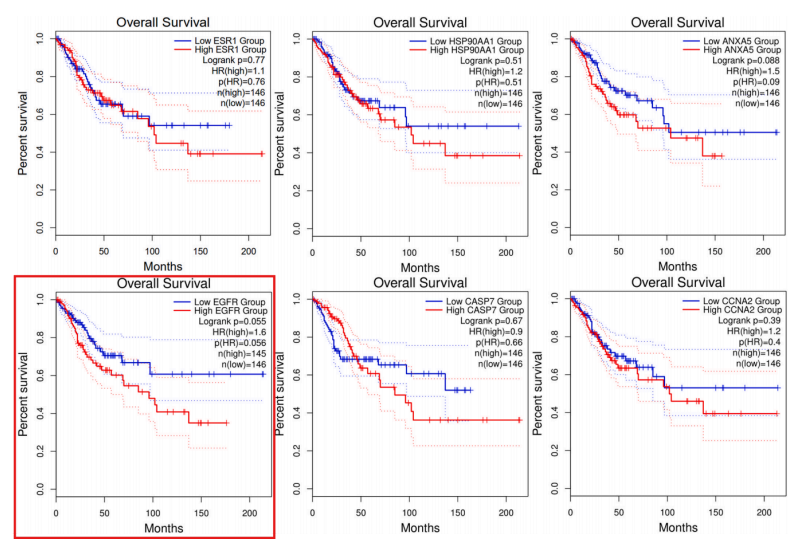
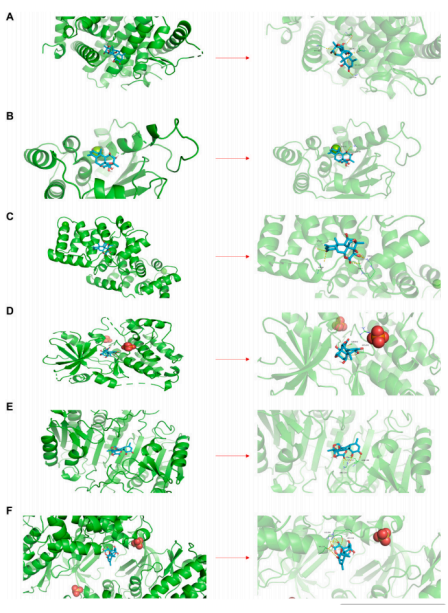


Fig 3. **Survival analysis**

Although all genes exhibited a p-value greater than 0.05, the **EGFR** gene had the smallest p-value among them.



Receptor	Binding energy (KJ/mol)
ESR1	−7.0
HSP90AA1	−7.0
ANXA5	−6.8
EGFR	−7.5
CASP7	−7.2
CCNA2	−7.3

Fig 4. **Molecular docking** analysis

BD and EGFR showed the minimal binding energy

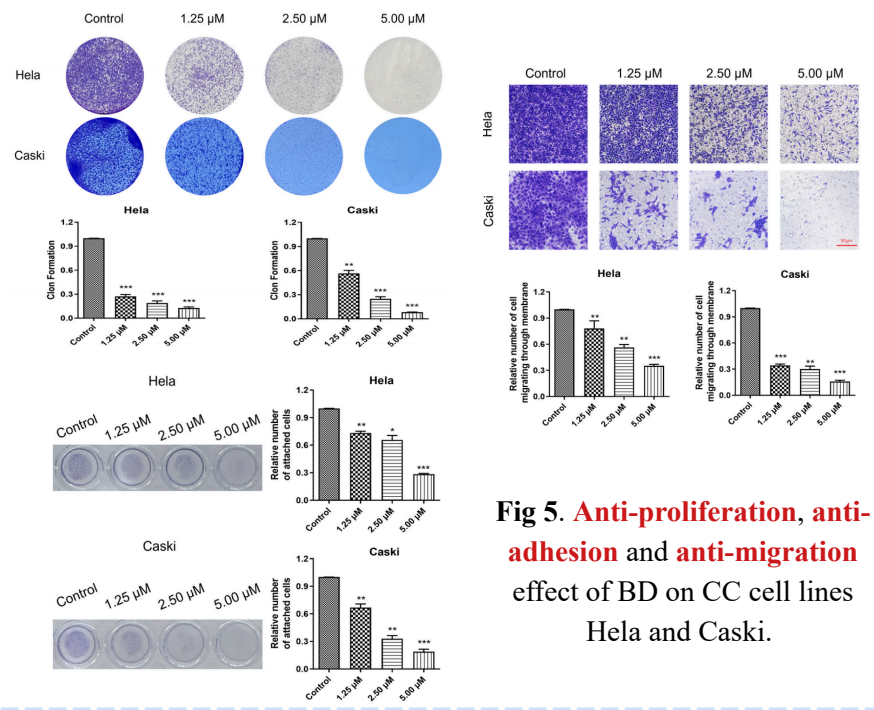


Fig 5. **Anti-proliferation**, **anti-adhesion** and **anti-migration** effect of BD on CC cell lines Hela and Caski.

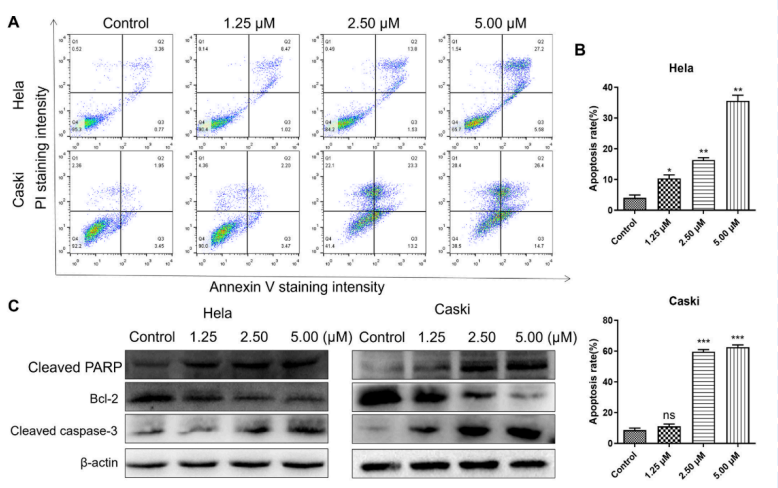
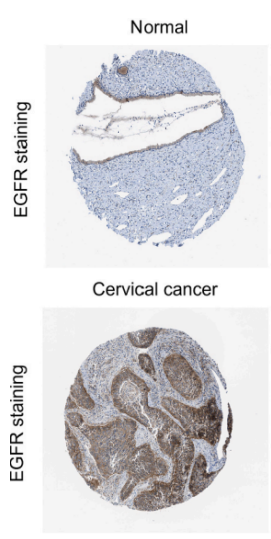


Fig 6. Effect of BD on **apoptosis** in CC cell lines Hela and Caski.



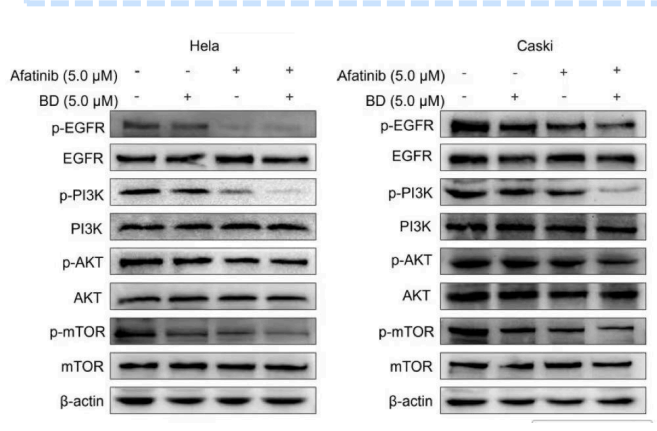


Fig 7. BD treatment effects on the **EGFR pathway** in Hela and Caski cells.

Conclusions

- This study illuminates BD as a **novel EGFR pathway modulator** with multi-layered anticancer mechanisms in cervical cancer. By bridging **computational predictions** with f**unctional validation**, we provide a robust framework for developing BD-based therapeutic strategies.
- The results from our study illustrate that BD boasts diverse anti-tumoral actions, encompassing the inhibition of cell **proliferation, adhesion, and migration**, alongsiden triggering **programmed cell death**, with a notable focus on its interaction with the **EGFR signaling pathway**.
- Molecular docking studies, coupled with the observed synergistic effect with the EGFR inhibitor afatinib,highlight BD's potential as a **targeted therapeutic agent**.
- Such convincing evidence highlights the critical need for expanded experimental scrutiny both in controlled environments and living organisms to corroborate the reliability of BD as a **viable treatment option** and elucidate its molecular mechanisms, thereby paving the way for its **future preclinical and clinical applications** in targeted cancer therapy.

References

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