

# 58P-Spectrum of Germline Pathogenic Mutations in 1087 Chinese Patients With Biliary tract cancer

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## BACKGROUND

- Biliary tract cancer(BTC) is a heterogeneous solid tumor with poor prognosis and the incidence of BTC is rising globally. In recent years, researchers have tried to identify therapeutic targets of BTC patients (pts), but have ignored the germline mutation landscape. Herein, we will present an overview regarding the status of pathogenic germline mutations in Chinese BTC pts.

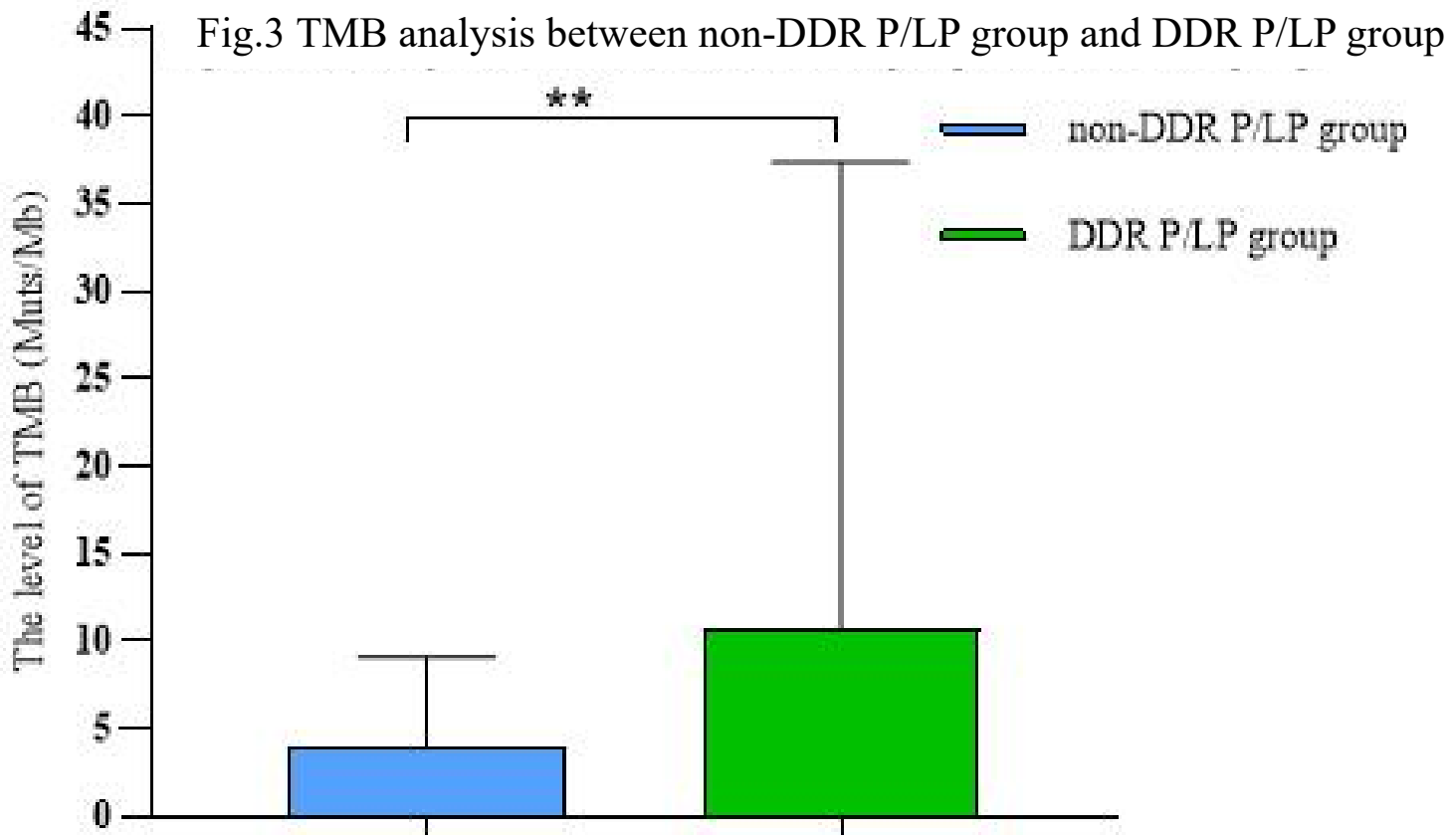
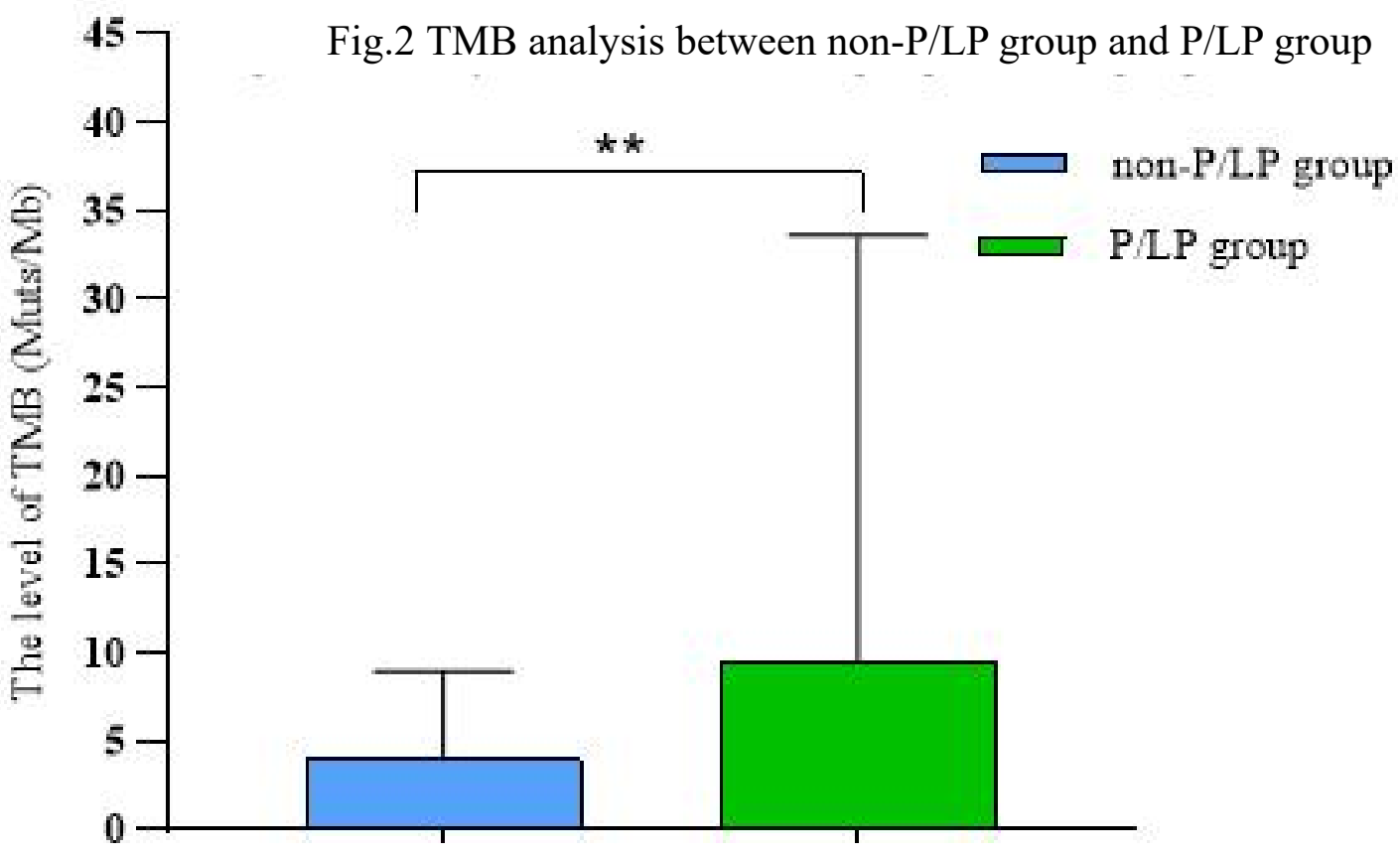
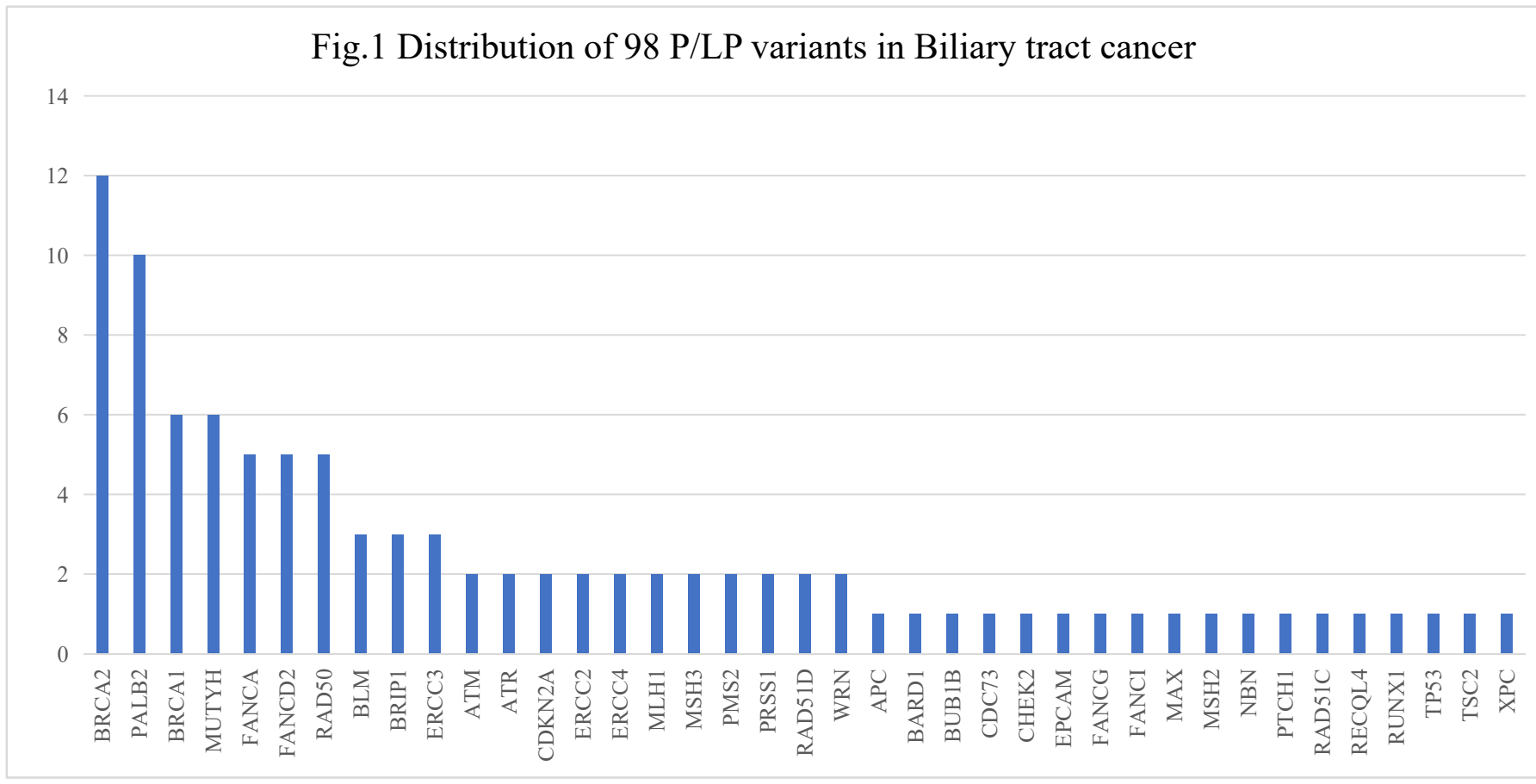
## METHODS

- We retrospectively analyzed 1087 Chinese BTC samples which underwent hybridization capture based nextgeneration sequencing (NGS) to investigate the prevalence of germline mutations. The pathogenicity of germline mutations (including SNV, small INDEL) was categorized based on American College of Medical Genetics and Genomics (ACMG) guidelines.

## RESULTS

- Of 1087 BTC pts, 94 (9.84%) pts were identified to carry 98 pathogenic variants (P) or likely pathogenic variants (LP) in 112-cancer predisposition gene panel, 4 pts carried 2 germline mutations. The rest 994 BTC pts were Non-P/LP group. No significant differences were found between P/LP and Non-P/LP groups in age (average age: 60.4 vs 61.8,  $p=0.2$ ). Most P/LP mutations were loss of function (LOF) variants.
- The highest prevalence of germline mutation was found in *BRCA1/2* ( $n=16$ , 1.47%), *PALB2*( $n=10$ , 0.92%), *MUTYH*( $n=6$ , 0.55%), *FANCA* ( $n=5$ , 0.46%) and *FANCD2*( $n=5$ , 0.46%) (Fig.1). On the contrary, somatic mutation analysis found that P/LP group exhibited significantly high tumor mutation burden (TMB) compared with non-P/LP group (average TMB: 9.50 vs 3.98,  $p < 0.001$ )(Fig.2).
- 71 BTC pts (6.7%) had germline mutations in the DNA-damage repair (DDR) signal pathway, of which homologous recombination (HR) genes accounted for the highest proportion. There was no age difference between DDR P/LP and non-DDR P/LP group (average age: 60.6 vs 61.8,  $p=0.34$ ). Compared with non-DDR P/LP group, individuals with DDR P/LP group tended to have a higher level of TMB (average TMB: 10.66 vs 4.01,  $p < 0.001$ )(Fig.3).

## FIGURES



## CONCLUSIONS

- This research elucidated the spectrum of pathogenic germline mutations in Chinese BTC to identify candidate genes for hereditary BTC. In addition, the occurrence of DDR P/LP germline mutations were significantly correlated with a higher TMB, which could lead to an improvement in the personalized treatment for BTC pts.