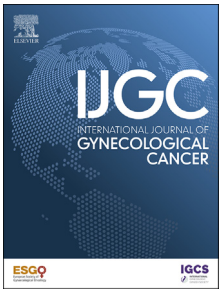
LETTER

Correspondence on "Large-scale analysis to identify risk factors for ovarian cancer" by Madakkatel et al



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Madakkatel and colleagues[1] (2025) identified ovarian cancer predictors from 2920 features using a CatBoost Gradient Boosting Decision Tree (GBDT) and SHapley Additive exPlanations (SHAP) values. However, their methodology raises concerns about model bias and the reliability of feature importance. It is a common misconception that even highly accurate machine learning models like GBDT, despite strong predictive performance, reliably yield trustworthy feature rankings. This principle is widely recognized, and validated by over 300 peer-reviewed articles (details in Supplementary Material). Boosting algorithms often produce biased importance scores by overemphasizing features used in early splits.[2] SHAP values, used for explainability, inherit and may amplify these biases.[3] This "GBDT-SHAP pipeline" distorts interpretation, increasing the risk that features reflect model artifacts, not true causal drivers. Moreover, validating feature importance is inherently difficult due to the absence of ground truth, undermining the stability and reproducibility of findings. To address these concerns, we advocate for multi-faceted analytical strategies that combine machine learning with robust statistical validation methods. For instance, approaches like highly variable gene selection and feature agglomeration can better capture complex, latent patterns in the data.[4,5] Integrating such methods alongside machine learning is essential for generating reliable insights in health risk assessment, ensuring findings are not only predictive but also interpretable and reproducible.

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Souichi Oka[a,*] **Yoshiyasu Takefuji**[b]

[a]*Research and Development Planning Department, Science Park Corporation, Kanagawa, Japan*
[b]*Musashino University, Faculty of Data Science, Tokyo, Japan*

[*]***Correspondence to*** *Dr Souichi Oka, Science Park Corporation, 3-24-9 Iriya-Nishi Zama-shi, Kanagawa, Japan.*
E-mail: souichi.oka@sciencepark.co.jp (S. Oka)

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