Discovery of CD200R1 as a Novel Immuno-oncology Target Using Pleiotropic Signals From 23andMe’s Genetic and Health Survey Database

Xin Fang*, Wei-Jen Cheng†, Jill Fenaux, Alice Chen, Nizar Batada, Malke Schmidt, Sophia R. Majed, Sushil Kumar, Steven Plitts

23andMe, Inc. South San Francisco, CA.
*Presenting author.
†These authors contributed equally to this poster.

BACKGROUND

Identifying a pleotropic signature.

- Using a genome-wide association study (GWAS) across multiple phenotypes to assess "immuno-oncology (IO) signature.

- A coding variant of the immunosuppressive protein CD200 (rs140763487) serves as a proof of concept (Figure 1).

- To identify novel potential targets for cancer therapies with human genetic support, we used a genome-wide association study (GWAS) across multiple phenotypes to assess the direction of effect in cancer and immune diseases (Figure 2).

- The authors contributed equally to this poster: X.F. performed the analysis on gene expression and generated the poster; W-J.C. performed the pleiotropy analysis, gene expression analysis, and identified genetic signatures.

METHODS AND RESULTS

CD200R1 was identified as a potential IO target, as 3 components of the pathway were found to have an IO signature in the 23andMe database.

- At an IO signature was observed for 3 genes known to be involved in the same immune pathway: CD200R1, CD200 (IO signature), and DOK2 (involved in CD200R1/CD200 signaling pathway).

- The frequency and level of CD200R1 expression were examined on TIL subsets from 32 ICI non-responders among 23andMe.

- A positive correlation (ranging from 0.51-0.88) between CD45 and CD200R1 expression in TILs was identified for all ICI non-responders.

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CONCLUSIONS

- There are multiple instances in the 23andMe database where genetic associations driven by a common causal variant are observed to consistently show opposing direction of effect in cancer and immune diseases—an pleotropic IO signature.

- CD200R1 was identified as a critical immune checkpoint inhibitor (ICI) non-responders.

- The safety, pharmacokinetics, and anti-cancer activity of 23ME-006 is currently being evaluated in patients with advanced solid tumors in a phase 1 clinical trial (ClinicalTrials.gov Identifier: NCT09510212).

REFERENCES

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SUPPORT

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