## Life Science

# Mathematical Analysis of Tumor Immune Escape in Colorectal Cancer

https://haenolab.jp/en/

Hiroshi Haeno
Associate Professor, Research Institute for Biomedical Sciences, Tokyo University of Science.
haeno@rs.tus.ac.jp

## Our mission

Our mission is mathematical formulation of diseases by differential equation systems and stochastic models. Recent advancement of measurement technology and computer performance in biological and medical research field enables us to develop verifiable theoretical models based on large and high precision data. We are motivated to propose (i) principles; (ii) drug targets; (iii) prognosis prediction; and (iv) optimal treatment strategies of diseases. Please feel free to contact us if you are interested.
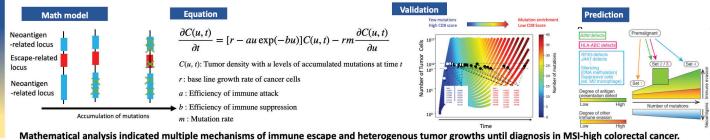
## Purpose of Research

Microsatellite instability-high (MSI-H) colorectal cancer has demonstrated efficacy with immune checkpoint inhibitors to a certain extent; however, the response is not universally observed among all patients, highlighting the need for establishing methods to predict treatment efficacy.

## Summary of Research

We developed a mathematical model of tumor evolution under the selective pressure of immune responses. We recapture 3E concept in tumor immune, i.e., tumor increases exponentially at first (when ), gradually slows down, then may even decrease in number because of the immune responses, and finally increase again after the successful immune evasion. Moreover the model predicted two distinct tumor subtypes with low or high mutations, which should have different potential against immunotherapy.

**Mathematical analysis of cancer immunoescape in MSI-high colorectal cancer** (Kawazu et al. Gastroenterology 2021)



**Math model**

Neoantigen-related locus
Escape-related locus
Neoantigen-related locus

Accumulation of mutations

**Equation**

$$\frac{\partial C(u,t)}{\partial t} = [r - au\exp(-bu)]C(u,t) - rm\frac{\partial C(u,t)}{\partial u}$$

$C(u,t)$: Tumor density with $u$ levels of accumulated mutations at time $t$

$r$ : base line growth rate of cancer cells

$a$ : Efficiency of immune attack

$b$ : Efficiency of immune suppression

$m$ : Mutation rate

**Validation**

**Prediction**

Mathematical analysis indicated multiple mechanisms of immune escape and heterogenous tumor growths until diagnosis in MSI-high colorectal cancer.

### Points

Mathematical Modeling of Tumor Progression with Immune Responses

- Suggest a conceptual model that describes the tumor evolution under the pressure of immune responses.
- Explain the emergence of tumors that have high/low mutational load.
- Examine the therapeutic effect by computational simulations of cancer treatment.

## Future Developments

- Development of Agent Based Model to consider intratumor heterogeneity and validate with clinical data .
- Prediction of Immune Checkpoint Inhibitor Treatment Based on the Mathematical Analysis.
- Suggestion of Optimal Treatment Strategies for Colorectal Cancer Based on the Mathematical Analysis.