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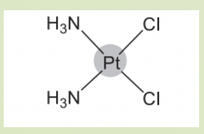
Development of evaluation model of flow cytometry for combination effects of anti-cancer agents using machine learning

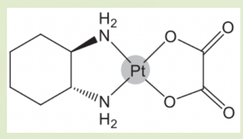
Koki Murayama [1] Ying Tong [1] Barkha Saraswat [1] Kohei Hayashi [1 2] Mitsuko Masutani [1]
Center for Bioinformatics and Molecular Medicine Nagasaki University Graduate School of Biomedical science [1]
Department of Gastroenterology and Hepatology, Nagasaki University Graduate School of Biomedical Sciences[2]

INTRODUCTION & AIM

Cisplatin and oxaliplatin



Cisplatin (CDDP): Binds to biological components, causes crosslinks of DNA and proteins and inhibits DNA strands break repair



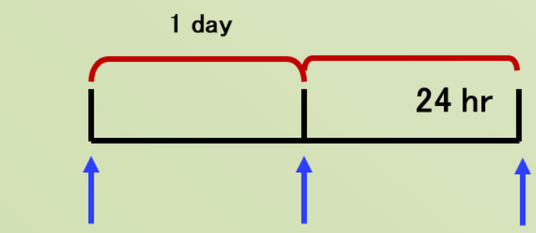
Oxaliplatin (LOHP) : Like cisplatin, it is a platinum preparation with platinum atoms, and differs from cisplatin in terms of action and side effects.

	Mechanism of Action	Major Side Effects
CDDP	Inhibits DNA replication and synthesis (S phase)	Renal toxicity, hearing impairment
LOHP	Inhibits transcription and translation (M phase)	Peripheral neuropathy

Our previous studies have shown a synergistic effect of LOHP and CDDP on cytotoxicityof particular gastric cancer cells. However, methods for analysing the combined effects of anticancer drugs remain limited.
We aimed to use machine learning to create a more applicable evaluation model of the combination effect data of anticancer drugs by flow cytometry (FCM) utilizing information of cell cycle distribution and cell states.

METHODS

Flow cytometry (FCM) Process



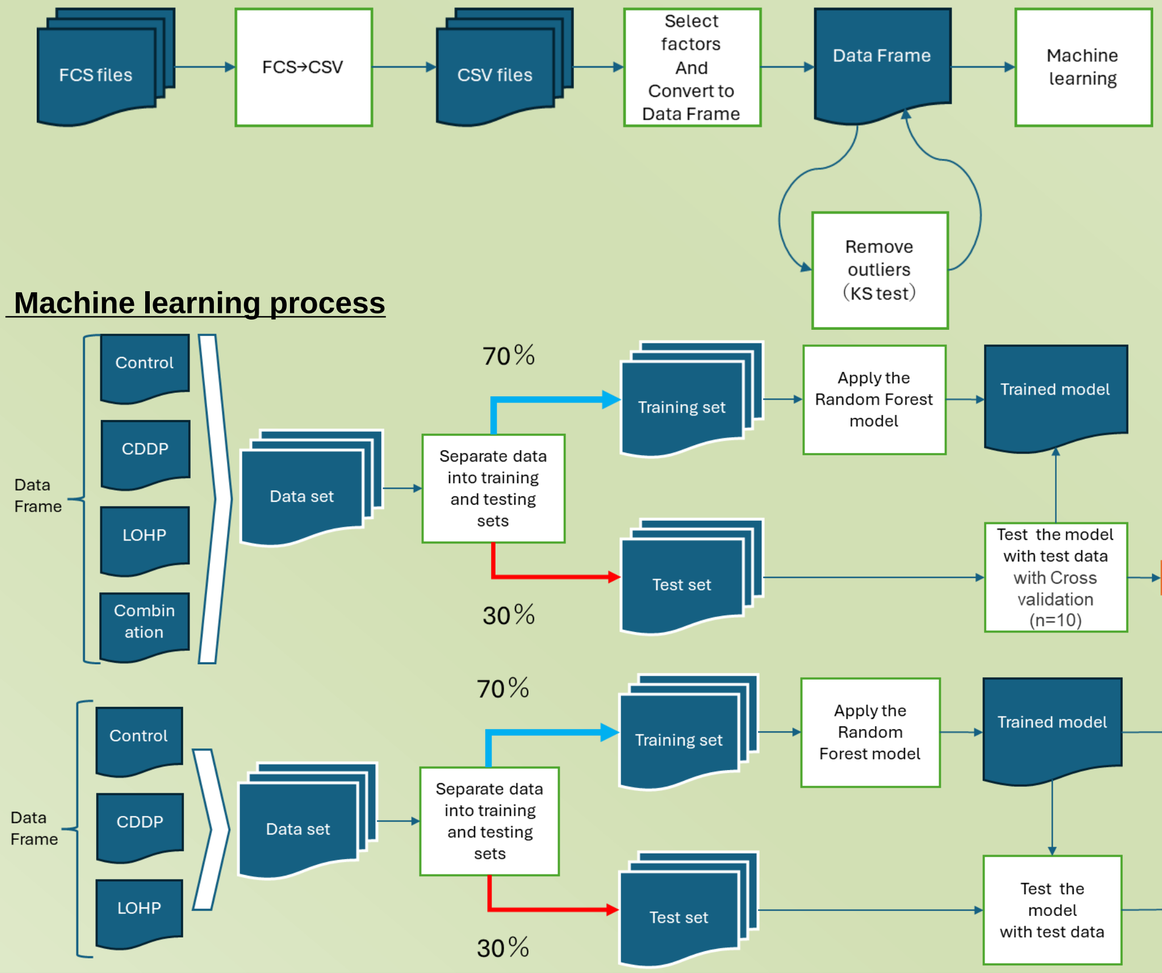
MKN45
MKN28
KATOⅢ
cell seeding

CDDP
LOHP
CDDP / LOHP

Flow Cytometry
↓ 70% ethanol fixation
↓ RNase A treatment
↓ Propidium iodide (PI) staining
↓ Flow cytometry (FSC, SSC, PI)
MKN45, KATOⅢ (n = 100)
MKN28 (n = 50–75)

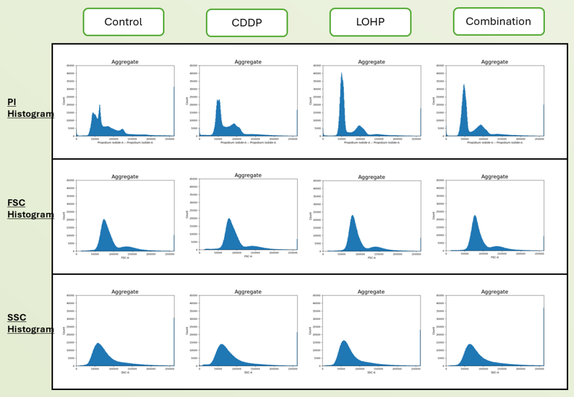
PI: the amount of cellular DNA
FSC: Cell size
SSC: Complexity of intracellular structures

Pre-processing process

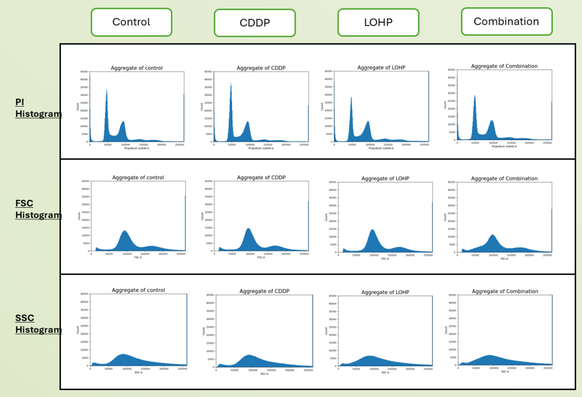


RESULTS & DISCUSSION

MKN45 histogram



KATOⅢ histogram



Accuracy of test model with 4 conditions

Cell line	Factor	Score (mean ± SE)
MKN45	PI	0.954 ± 0.010
	FSC	0.890 ± 0.010
	SSC	0.959 ± 0.010
MKN28	PI	0.977 ± 0.010
	FSC	0.995 ± 0.005
	SSC	0.923 ± 0.029
KATOⅢ	PI	0.964 ± 0.010
	FSC	0.835 ± 0.011
	SSC	0.861 ± 0.012

Judgement for Combination

Cell line	Factor	Model score	Judgement for combination
MKN45	PI	0.979	{'LOHP': 98, 'control': 2}
	FSC	0.949	{'LOHP': 48, 'control': 47, 'CDDP': 1}
	SSC	0.860	{'CDDP': 59, 'control': 34, 'LOHP': 4}
MKN28	PI	1	{'control': 57, 'CDDP': 19}
	FSC	0.958	{'CDDP': 64, 'control': 9, 'LOHP': 3}
	SSC	1	{'CDDP': 58, 'control': 32, 'LOHP': 7}
KATOⅢ	PI	0.989	{'CDDP': 54, 'control': 13, 'LOHP': 9}
	FSC	0.963	{'LOHP': 50, 'CDDP': 41, 'control': 6}
	SSC	0.933	{'LOHP': 78, 'CDDP': 17, 'control': 1}

CONCLUSION

- Combining flow cytometry (FCM) with machine learning enables more objective analysis of the combined effects of anticancer drugs
- Using PI data, the developed random forest model distinguished between control group, CDDP alone, LOHP alone, and combination group with over 95% accuracy
- The effect of drug combination showed tendencies similar to either CDDP or LOHP alone, depending on the cell line and measurement factor

FUTURE WORK / REFERENCES

- This method shows promise as a new approach for evaluating the combined effects of anticancer drugs
- FSC and SSC, which have only been used supplementarily until now, can become useful factors when using machine learning

COI Disclosure Information
Lead Presenter: Koki Murayama Principal Researcher: Mitsuko Masutani We have no financial relationships to disclose.

https://sciforum.net/event/CELLS2025