Simultaneous Impedance and OCR Measurements Reveal Complementary Cellular Responses to Cisplatin in A549 Cells

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Abstract

In this study, the CIMFS-96 system developed by CELLAMES Inc. was used in combination with the Resipher system from Lucid Scientific, Inc. to measure changes in impedance and oxygen consumption rate (OCR) following cisplatin treatment in A549 cells. The relationship between OCR and impedance measurements was then evaluated.

Following treatment with cisplatin at different concentrations (0, 1, 10, and 100 μM), OCR and impedance showed similar cisplatin-induced response trends. However, because OCR primarily reflects mitochondrial oxidative metabolism whereas impedance reflects cell adhesion and morphology, the two measurements should be interpreted as complementary readouts rather than directly proportional parameters.

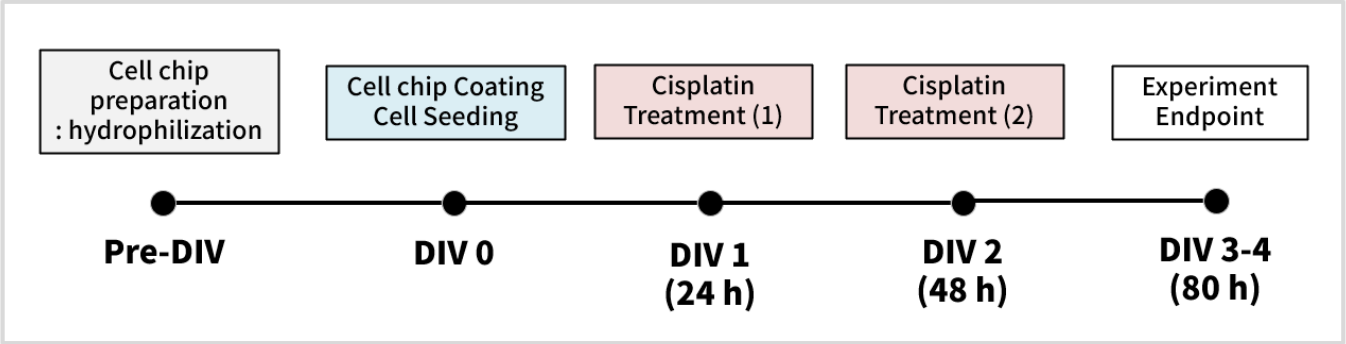
In addition, overall impedance profiles were comparable between conditions with and without Resipher-based OCR measurements, suggesting that the influence of Resipher measurements on impedance analysis was limited. Impedance measurements also reflected morphology-related changes observed in brightfield images, including changes in cell spreading and cell-electrode coverage, indicating that impedance analysis can provide additional information not directly captured by OCR data. OCR response profiles were similar between ITO electrode-based cell chips and SUS316L electrode-based PCB cell chips, suggesting that the differences in the electrode/substrate configurations had limited influence on OCR measurements under the tested conditions.

Taken together, these findings suggest that the combined use of OCR and impedance measurements may provide a complementary approach for evaluating drug-induced cellular responses.

Experimental Overview

Cell Type	A549 cell line	**Seeding Density**	15,000 cells/well
System	CIMFS-96 (CELLAMES Inc.) Resipher (Lucid Scientific, Inc.)	**Cell Chip**	ITO electrode-based cell chips (CITO-16W01E-IFE; ITO) × 2 SUS316L electrode-based PCB cell chips (CPCB-16W01E-IFE; PCB) × 2
Coating Reagent	Poly-D-lysine	**Treatment**	Cisplatin 0, 1, 10, and 100 μM

Experimental Flow



Cell Chip Hydrophilization (Pre-DIV)

- ITO electrode-based cell chips (CITO-16W01E-IFE) and SUS316L electrode-based PCB cell chips (CPCB-16W01E-IFE) were hydrophilized one day prior to cell seeding.

Cell Preparation (DIV 0)

- Wells were coated with 50 µg/mL Poly-D-lysine.
- A549 cells were seeded onto both ITO electrode-based cell chips and SUS316L electrode-based PCB cell chips at 15,000 cells/well. Cells were cultured in a humidified incubator at 37°C and 5% CO_2.
- One hour after cell seeding, cell attachment was confirmed, and OCR and impedance measurements were initiated.

First Cisplatin Treatment (DIV 1, 24 h)

- At 24 h after cell seeding, A549 cells were treated with cisplatin at different concentrations (0, 1, 10, and 100 µM).
- Brightfield images were acquired at the same time point.

Second Cisplatin Treatment (DIV 2, 48 h)

- At 48 h after cell seeding, a second cisplatin treatment was performed under the same concentration conditions with a half-medium change.
- Brightfield images were acquired at the same time point.

End of Experiment (DIV 3–4, 80 h)

- OCR and impedance measurements were continued until 80 h after cell seeding.
- OCR and impedance profiles, along with brightfield images, were analyzed to assess cisplatin-induced cellular changes.

Results

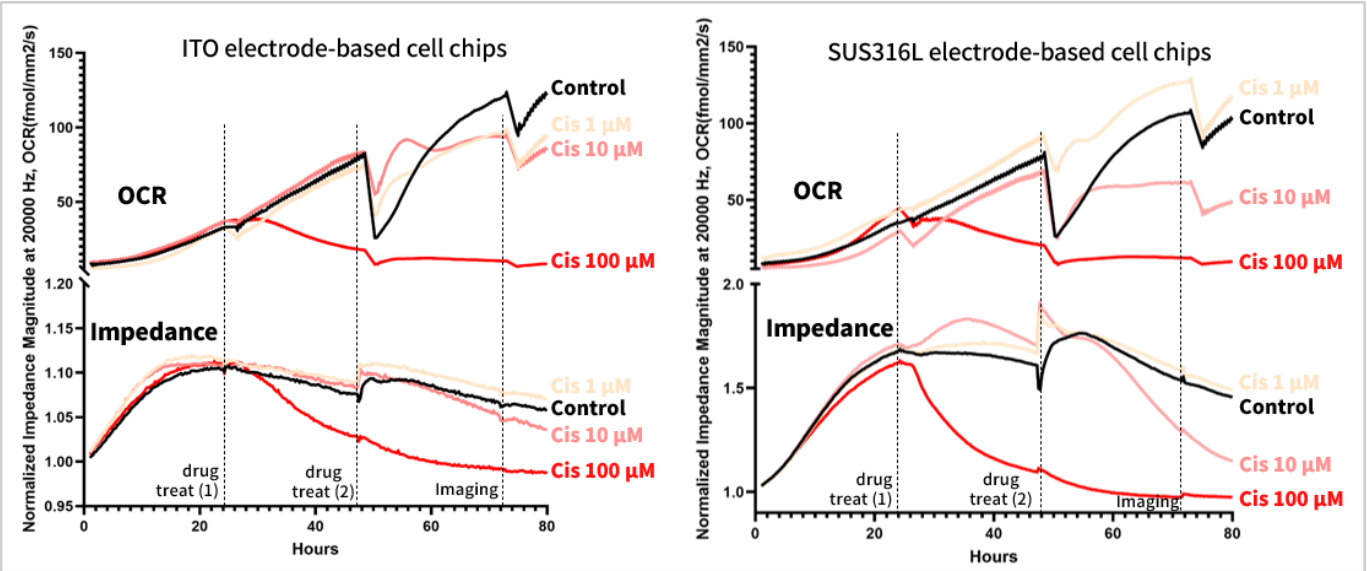


Figure 1. Changes in OCR and impedance profiles following cisplatin treatment in ITO and SUS316L electrode-based cell chips.

OCR and impedance were monitored in A549 cells cultured on ITO electrode-based cell chips and SUS316L electrode-based PCB cell chips following treatment with cisplatin at different concentrations (0, 1, 10, and 100 μM). Vertical dashed lines indicate the timing of the first cisplatin treatment, second cisplatin treatment, and imaging.

Following cisplatin treatment, OCR and impedance showed comparable response trends in both cell chip types. In the control, 1 μM, and 10 μM groups, OCR generally increased or was maintained during the measurement period, whereas the 100 μM group showed a marked reduction in OCR. Similarly, impedance profiles showed relatively gradual changes in the control, 1 μM, and 10 μM groups, while the 100 μM group showed a clear decrease in impedance.

Although OCR and impedance showed similar overall drug-response trends, the detailed temporal profiles were not identical. This difference is likely because each measurement reflects distinct biological properties, as OCR primarily reflects mitochondrial oxidative metabolism, whereas impedance reflects cell adhesion and morphology. Therefore, OCR and impedance measurements should be interpreted as complementary readouts for evaluating cisplatin-induced cellular responses rather than as directly proportional parameters.

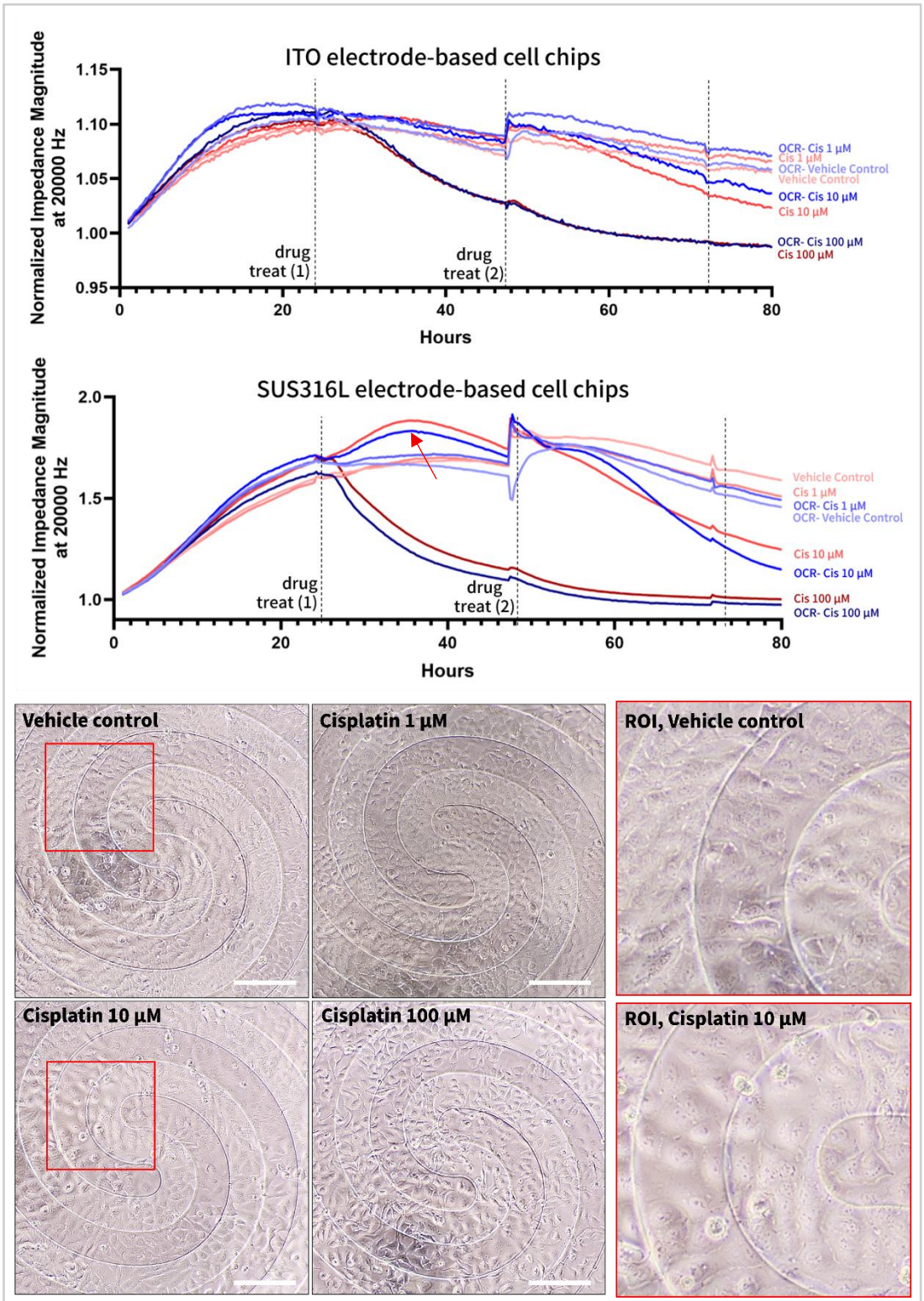


Figure 2. Impedance profiles with and without Resipher-based OCR measurements.

Impedance profiles were compared between conditions with and without Resipher-based OCR measurements in ITO electrode-based cell chips and SUS316L electrode-based PCB cell chips. The displayed brightfield images were acquired after the first cisplatin treatment to assess morphological changes induced by the initial drug exposure. Red boxes indicate the regions selected for magnified views, and the right panels show magnified ROIs from the vehicle control and cisplatin 10 μM groups. Scale bars = 200 μm.

Overall, impedance profiles were comparable between conditions with and without Resipher-based OCR measurements, suggesting that the influence of Resipher measurements on impedance analysis was limited. Notably, in SUS316L electrode-based PCB cell chips, an increase in impedance was observed in the cisplatin 10 μM group after the first drug treatment (red arrow). Brightfield images acquired at 48 h showed that cells in the cisplatin 10 μM group exhibited a more flattened and spread morphology compared with the vehicle control group, which may have increased cell–electrode coverage and contributed to the observed impedance increase.

These results indicate that impedance measurements can reflect cisplatin-induced morphological changes that may not be directly captured by OCR measurements. Therefore, impedance analysis can provide complementary information to OCR data when evaluating drug-induced cellular responses.

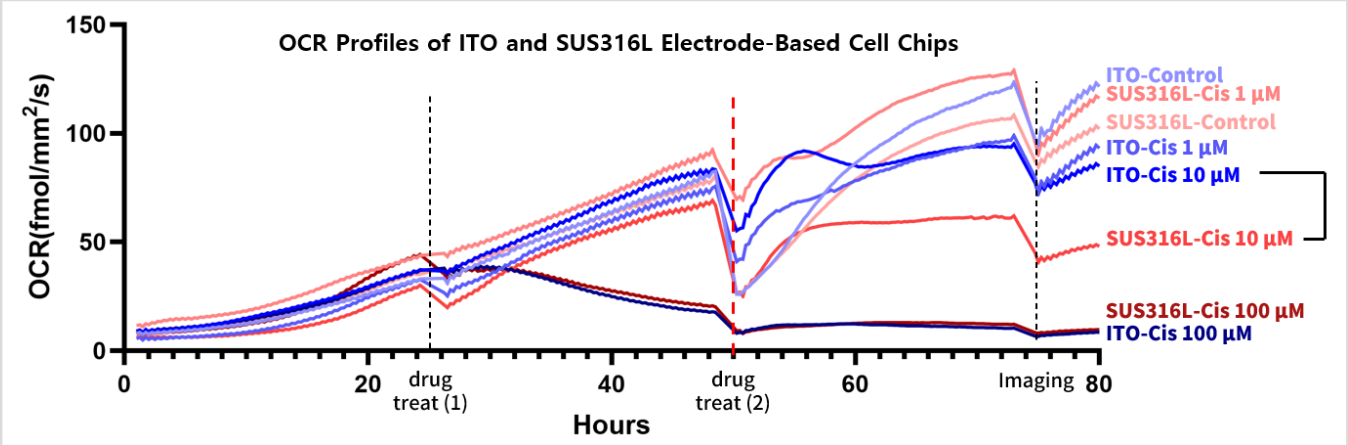


Figure 3. Comparison of OCR profiles between ITO and SUS316L electrode-based cell chips.

OCR profiles measured using the Resipher system were compared between ITO electrode-based cell chips and SUS316L electrode-based PCB cell chips following cisplatin treatment at different concentrations (0, 1, 10, and 100 μM).

Overall, OCR profiles were comparable between ITO and SUS316L electrode-based cell chips. A notable difference was observed in the cisplatin 10 μM condition at the end of the experiment, where the OCR value of the ITO group appeared higher than that of the SUS316L group. However, this apparent difference was mainly due to the differences in starting OCR levels immediately after the second cisplatin treatment. The red dashed line indicates the starting point used to compare OCR changes after the second drug treatment. At the endpoint of the cisplatin 10 μM condition, the OCR value of the ITO group was approximately 1.8-fold higher than that of the SUS316L group. However, when OCR changes were normalized to the starting OCR levels of the second cisplatin treatment, the relative difference decreased to approximately 1.07-fold.

Overall, OCR response trends were similar between ITO and SUS316L cell chips across the tested conditions. Therefore, the differences in the electrode/substrate configurations had limited influence on Resipher-based OCR measurements under the tested conditions.

Conclusion

In this study, combined OCR and impedance measurements were performed using the CIMFS-96 and Resipher systems to evaluate cisplatin-induced cellular responses in A549 cells. OCR and impedance showed similar response patterns following cisplatin treatment. However, because OCR and impedance represent different cellular properties, the relationship between the two measurements should not be interpreted as directly proportional.

Impedance profiles were comparable between conditions with and without Resipher-based OCR measurements, suggesting that the influence of Resipher measurements on impedance analysis was limited. In addition, impedance measurements reflected morphology-related changes observed in brightfield images, including changes in cell spreading and cell–electrode coverage, supporting their complementary value to OCR data. OCR profiles were generally consistent between ITO electrode-based cell chips and SUS316L electrode-based PCB cell chips, suggesting that the differences in the electrode/substrate configurations had limited influence on Resipher-based OCR measurements under the tested conditions.

Taken together, these findings suggest that OCR and impedance measurements exhibited similar drug-response trends while capturing distinct cellular properties. Their combined use can provide complementary information on mitochondrial oxidative metabolism, cell adhesion, and morphology, supporting a more comprehensive interpretation of drug-induced cellular responses. This supports the potential application of simultaneous OCR and impedance measurements in cellular response evaluation and drug screening.

Supplementary Data

- No supplementary data are available.

Keywords

CIMFS-96, Resipher, Oxygen consumption rate, Impedance, Cisplatin-induced cellular response