3D microfluidic ex vivo culture of organotypic tumor spheroids to model immune checkpoint blockade.

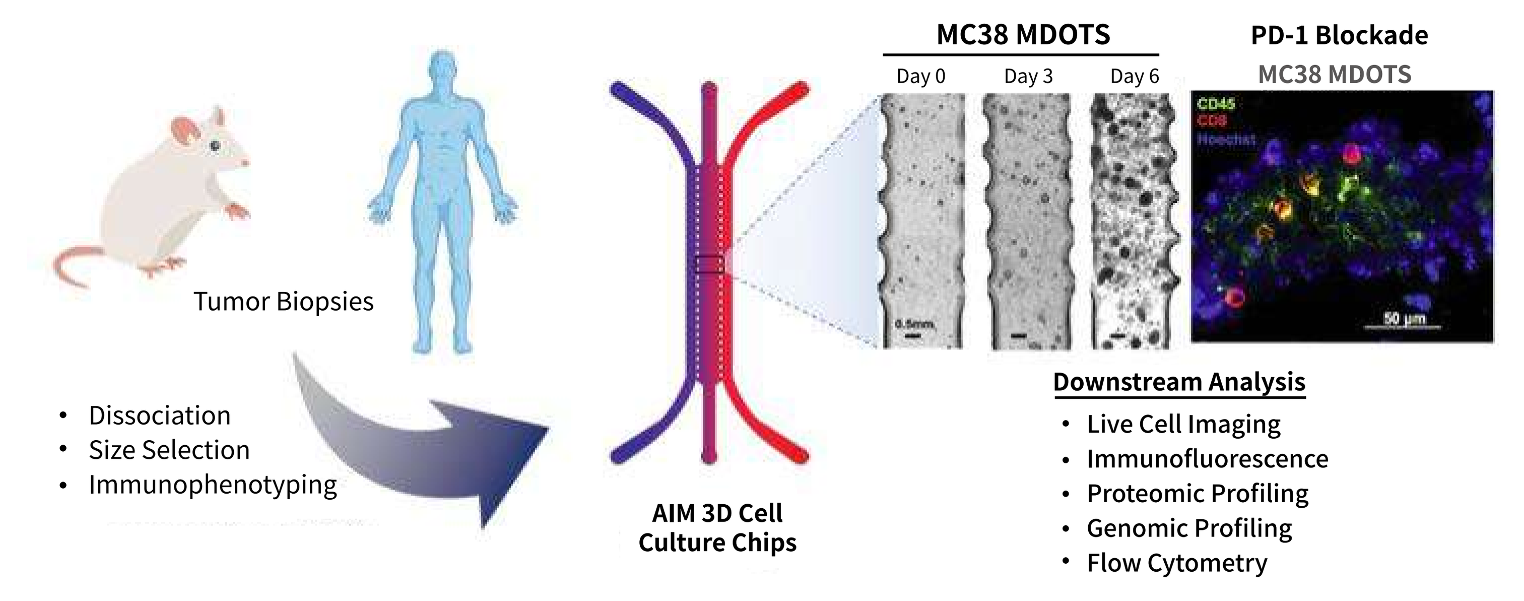
Aref AR1, Campisi M, Ivanova E, Portell A, Larios D, Piel BP, Mathur N, Zhou C, Coakley RV Bartels A, Bowden M, Herbert Z, Hill S, Gilhooley S, Carter J, Cañadas I, Thai TC, Kitajima S Chiono V, Paweletz CP, Barbie DA, Kamm RD, Jenkins RW.

Microfluidic culture has the potential to revolutionize cancer diagnosis and therapy. Indeed, several microdevices are being developed specifically for clinical use to test novel cancer therapeutics. To be effective, these platforms need to replicate the continuous interactions that exist between tumor cells and non-tumor cell elements of the tumor microenvironment through direct cell-cell or cell-matrix contact or by the secretion of signaling factors such as cytokines, chemokines and growth factors. Given the challenges of personalized or precision cancer therapy, especially with the advent of novel immunotherapies, a critical need exists for more sophisticated ex vivo diagnostic systems that recapitulate patient-specific tumor biology with the potential to predict response to immune-based therapies in real-time. Here, we present details of a method to screen for the response of patient tumors to immune checkpoint blockade therapy, first reported in Jenkins et al. Cancer Discovery, 2018, 8, 196-215, with updated evaluation of murine- and patient-derived organotypic tumor spheroids (MDOTS/PDOTS), including evaluation of the requirement for 3D microfluidic culture in MDOTS, demonstration of immune-checkpoint sensitivity of PDOTS, and expanded evaluation of tumor-immune interactions using RNA-sequencing to infer changes in the tumor-immune microenvironment. We also examine some potential improvements to current systems and discuss the challenges in translating such diagnostic assays to the clinic.

In vitro model을 이용한 immune checkpoint blockade assay에 관한 논문입니다. 아래 버튼을 클릭하시면 전문을 확인해 보실 수 있습니다

More information >>

Microfluidic chip을 이용한 in vitro 3D model



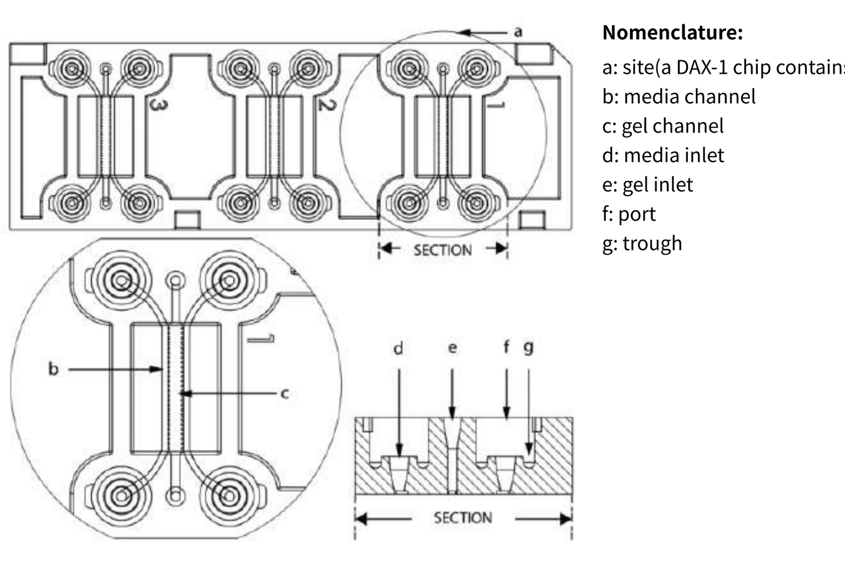
최근 몇 년간 immune checkpoint blockade(ICB) 요법이 성공했음에도 불구하고 선천적인 내성으로 인해 성공 case는 소수의 환자에 국한됩니다. Dual ICB, Anti-PD-1, Anti-CTLA4를 사용하는 combination therapy는 단일 요법보다 advanced melanoma에서 유의미한 결과를 보여주었습니다. Combination therapy의 조합 수가 계속 증가하고 있기 때문에, 이러한 요법의 효능을 적시에 전임상 및 임상적 환경에서 정확하게 예측할 수 있는 ICB의 분석이 필요합니다.
AIM biotech의 microfludic chip을 이용하여 연구중인 약물의 combination therapy를 in vitro model에서 분석해보시기 바랍니다.

Microfluidic chip

미세유체 칩은 미세유체 채널을 통해 유체를 흘려 보내 여러 가지 실험 조건을 동시에 수행할 수 있는 칩을 말합니다. 구체적으로, 플라스틱, 유리, 실리콘 등의 기판(또는 칩 재료)을 이용하여 미세 채널을 만들고, 이러한 채널을 통해 유체(예를 들어, 액체 시료)를 이동시킨 후, 미세유체 칩 내의 챔버에서 시료 분리, 세포의 혼합, 합성, 정량분석, 세포 증식 관찰 등을 할 수 있습니다. 이와 같이, 종래에 실험실에서 행해지던 실험들을 작은 칩 내에서 수행한다는 점에서, 미세유체 칩은 "랩-온-어-칩"(lab-on-a-chip)이라 불리기도 합니다.
기존의 미세유체 칩은 직접 제작하여 사용해야 했으나 최근에는 Ready-to-use 형태의 제품들이 출시되고 있습니다.
저희 웅비메디텍에서는 AIM Biotech 사의 AIM chip을 이용한 랩-온-어-칩 모델을 제안드립니다

General Information

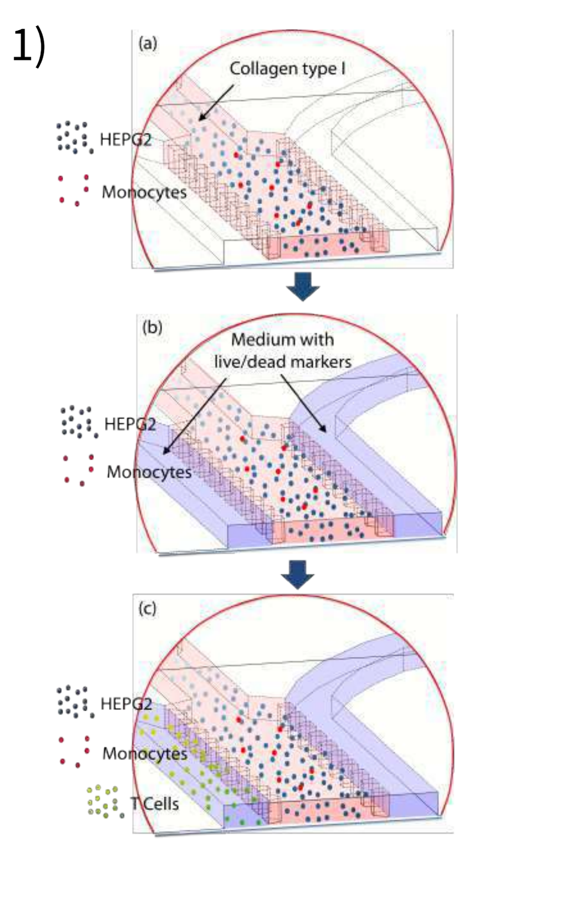
- Easy-to-Use
  - 상세 프로토콜 제공
- Real Time 현미경 관찰 가능
- 다양한 cell type co-culture 가능
- Flow control 가능
  - Interstitial flow
  - Shear flow
- Chemical gradients 가능



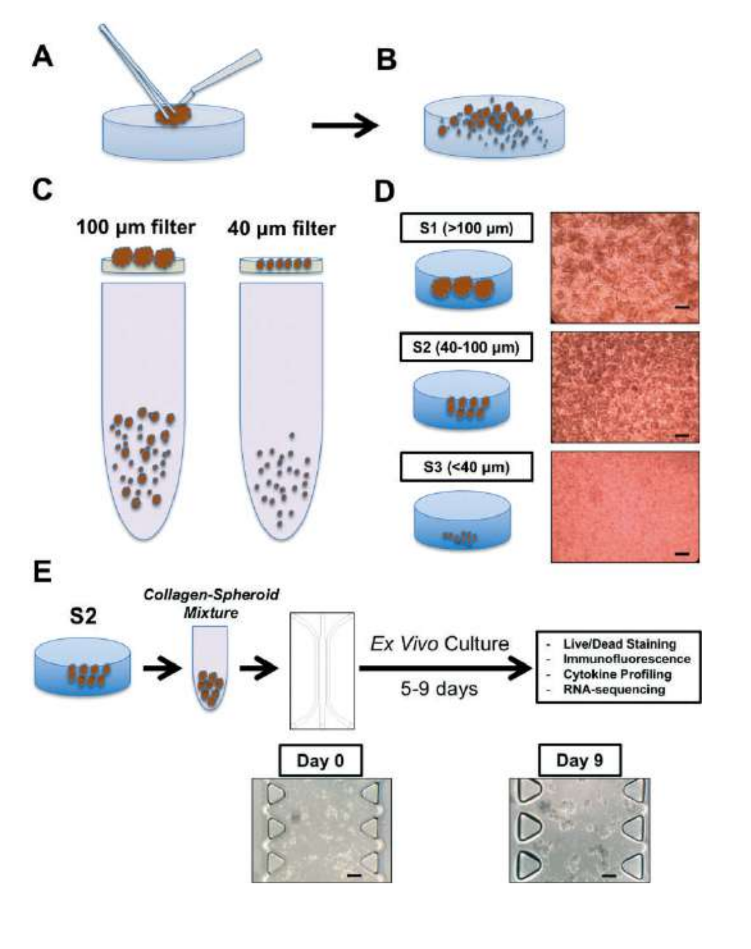
Nomenclature:
a: site(a DAX-1 chip contains 3 sites)
b: media channel
c: gel channel
d: media inlet
e: gel inlet
f: port
g: trough

Immunotherapy model

1)



2)



Cell line을 이용해 Tumor spheroid를 만든 뒤 immune cell들의 영향을 확인할 수 있습니다.
Patient-derived tumor 조직을 dissociation 한 뒤 size별로 filtering하여 chip 내에서 배양하였고, drug 처리 후 tumor의 영향을 확인할 수 있습니다

브로셔 01 >>

브로셔 02 >>

AIM chip – Ready-to-use microfluidic chip

Microfluidic devices for cell culture

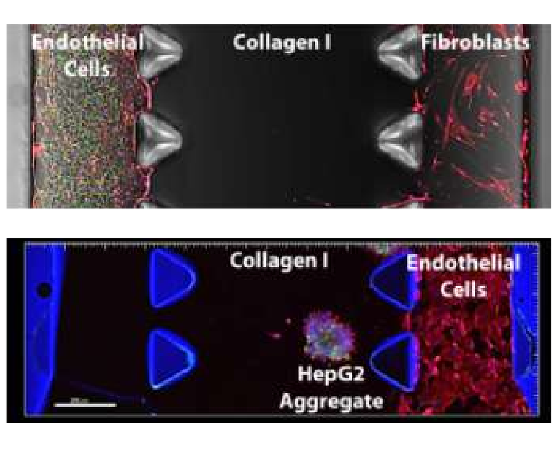
Using microfluidic technologies for 3D cell culture brings additional benefits:

- Microfluidic devices require small volumes of culture media and small quantities of cells, leading to reduced running costs. Studies can be conducted in cases where the cell source is limited (e.g. clinical samples)
- Microfluidic devices have Low space requirements given their small footprints, making it possible to scale up experimental throughput
- Compartmentalisation of cells into different channels/zones & live cell imaging analysis enable experimental designs with spatiotemporal elements

The underside of a microfluidic chip showing the size of its channels (250 microns deep). The chip is 25mm wide, measured from the edges shown above.

Multicellular culture made possible, with meaningful organization into models of biological systmes

The multi-channel design of AIM 3D Cell Culture Chips enables the co-culture of different cell types in distinct compartments in the device, yet allowing paracrine signalling between cell types to take place. the movement of cells between different channels (or within an individual channel) can be easily observed & tracked.
The growth and/or migration of cells within gel can often cause gel shrinkage or degradation. This problem is mitigated by the use of posts in AIM chips. The posts help to stabilize the gel and increase cell culture duration before the matrix collapses.

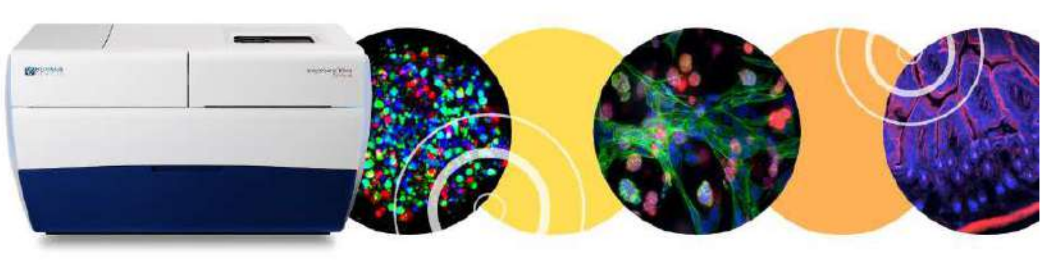


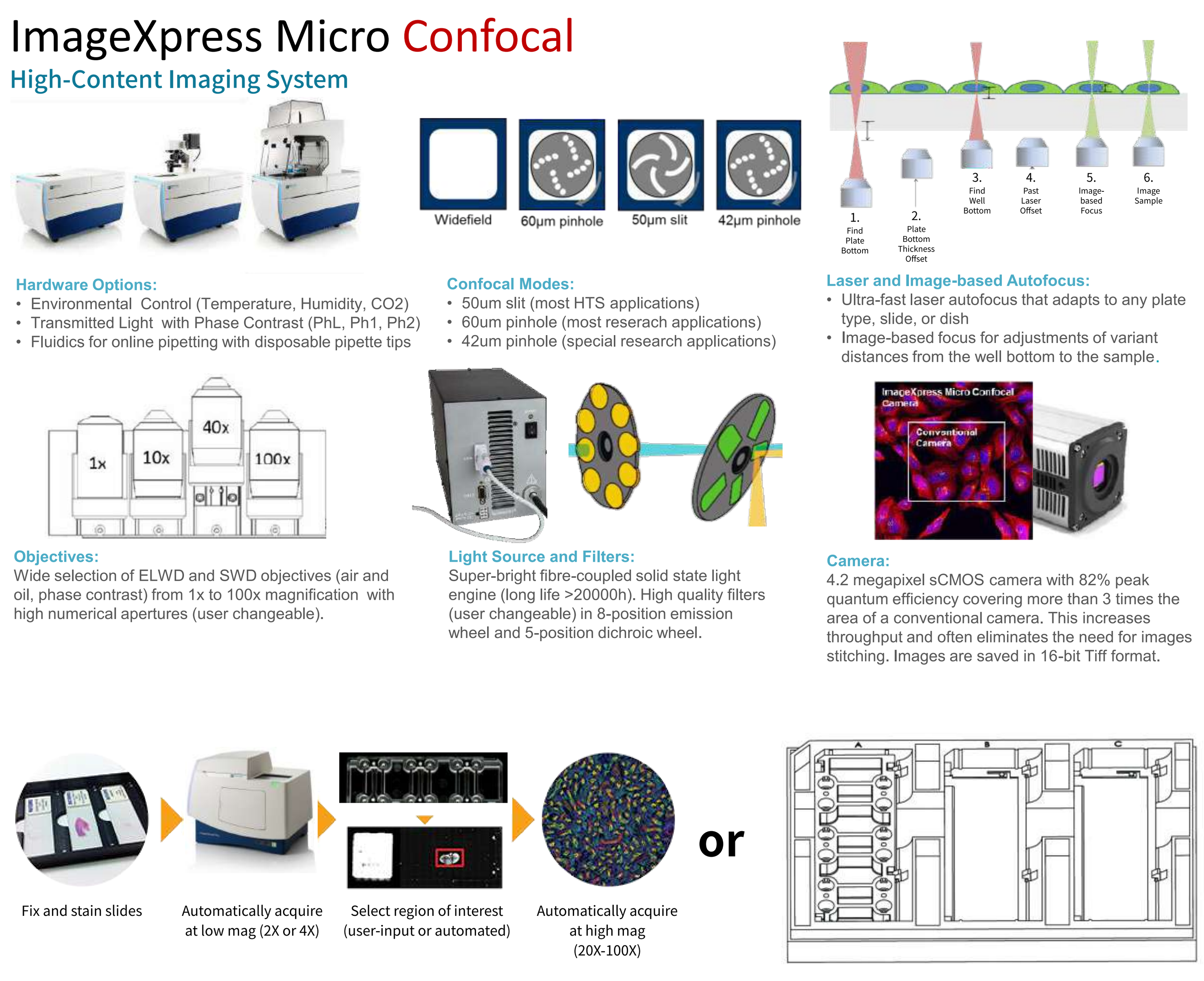
본사 홈페이지 확인 >>

웅비 브로셔 확인 >>

AIMchip with ImageXpress

MOLECULAR DEVICES





Molecular Devices의 ImageXpress는 high-contents imaging system으로 software를 이용하여 실험실 밖에서도 full-automation으로 사용하실 수 있는 장비입니다. MD만의 Laser and image-based dual-autofocus로 사용하시던 culture plate도 바로 적용이 가능하며, 분석 전용 software인 MetaXpress를 통해 자동으로 data를 분석합니다.
AIMchip은 slide glass 크기와 동일하게 제작되며, AIMchip의 holder는 96 well plate와 동일한 규격으로 제작됩니다.
MD ImageXpress의 slide-holder와 96-well plate holder를 이용하여 직접 디자인하신 랩-온-어-칩을 imaging과 동시에 분석해보세요.

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