Recent reports indicate that it takes nearly $800 million dollars and 10-15 years of development to bring a drug to market. Nearly 90% of the lead candidates identified by current in vitro screens fail to become marketable drugs. One of the reasons for the high failure rate of drug candidates is the lack of adequate models. To address the problem, we have developed a new cell culture analog amenable to routine use in drug development. It is based on the standard multiwell cell culture plate format but it provides perfused three-dimensional cell culture capability.

The multiwell plate microbioreactor array [1, 2] consists of a fluidic and a pneumatic manifold with a diaphragm sandwiched in between them. The fluidic manifold contains an array of microbioreactor and reservoir pairs (Figure 1). Each microbioreactor/reservoir pair is fluidically isolated from all other microbioreactors on the plate. A key component of a microbioreactor is a scaffold for tissue morphogenesis (Figure 2). The scaffold is a thin wafer containing an array of channels in which cells self-assemble into 3D pieces of tissue. It is backed by a filter and a support scaffold. Tissue in the scaffold is perfused by cell culture medium. The medium is re-circulated between the reactor and reservoir by a diaphragm pump. The diaphragms of all pumps and rectifying valves are actuated in parallel via three pneumatic lines distributed by the pneumatic manifold. Fluidic capacitors control flow pulsatility.

The system provides a means to conduct high throughput assays for target validation and predictive toxicology in the drug discovery and development process. It can be also used for evaluation of long-term exposure to drugs or environmental agents and as a model to study viral hepatitis, cancer metastasis, and other diseases and pathological conditions.