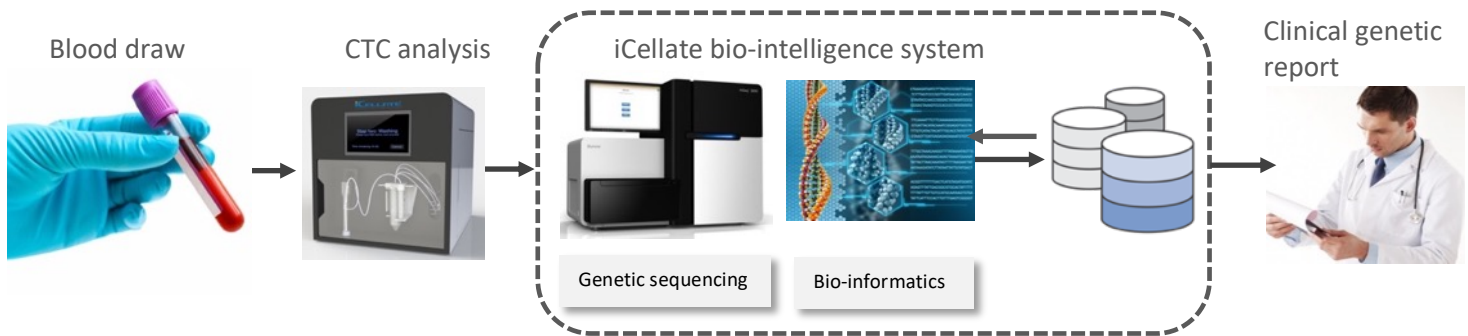
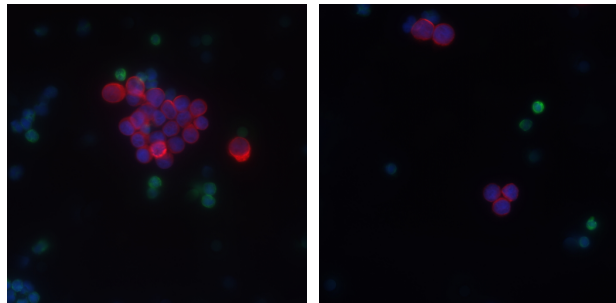


## Technical info sheet



### Technology

iCellate Medical has developed a proprietary Circulating Tumor Cell (CTC) isolation technology for scientific and clinical use, in response to the bias and therefore limited utility of the existing bio-marker based technologies. iCellate's CTC method is based on the general principle of negative selection for the "non-native blood cells" found in a standard blood sample, based on their robust deviant biomechanical properties. The selected cells are initially verified as authentic CTCs by the established definition of DAPI/keratin/CD45 immunostaining, and subsequently confirmed by genomic technologies designed to detect genetic aberrations indicative of cancer.



Red/blue = CTC, blue/green = leukocyte

The first of several challenges is to isolate the rare individual CTCs among 10 000 000 000 normal blood cells. iCellate has demonstrated under controlled conditions that not a single pre-defined sample is missed with high yield (90%), as one of very few, if not the only, companies.

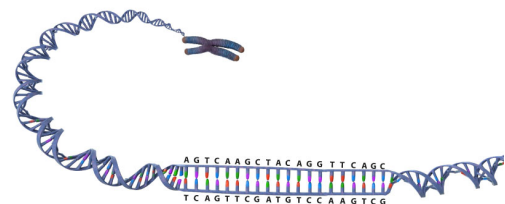
### Single cell sample preparation

Once the CTCs has been detected and isolated, the individual cells are then extracted by a proprietary preparation method also with high sensitivity and specificity, and in a state of preservation that preserves their information content and is technically compatible with genetic sequencing.

In a third step the isolated genetic material needs to be amplified by molecular biology so there are enough copies to match the requirements for Illumina next generation sequencing. iCellate uses an MDA-based (multiple displacement amplification) method to amplify extracted and purified genetic material from a single cell. It has been shown to be superior to other techniques. The MDA-method is PCR-free which minimizes the errors that are generated by PCR.

### Genetic sequencing – Bio-intelligence

The individual's somatic mutations associated with cancer are distinguished from the individual's germline-DNA sequence. Next generation sequencing is performed against a panel of the 468 most common, recognized, cancer mutations or subsets thereof. The final two steps in the iCellate solution is to first interpret the biological relevance of the large amount of data generated from sequencing, i.e. bioinformatics, and then to interpret the medical action ability and clinical relevance.



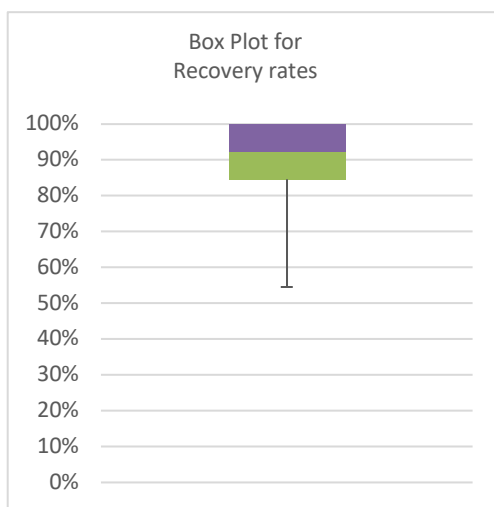
iCellate will establish an automated, self-learning, supervised bio intelligence pipeline that will:

- Establish that the cells are tumorous in nature, based on the overall genetic information
- Identifies a probable primary tumor location based on the pattern of sequence variations
- Provide individual treatment predictions, including for genetic eligibility for participation in clinical trials.

- Interrogates clinical outcomes information from own and other top-tier databases around the world
- Leverages all up-to-the-minute clinical outcomes data from the most similar patients around the globe to establish a new and better best practice
- Provide the state-of-the-art clinical genetic report, easily interpreted by the treating physician

## Laboratory verification

571 samples containing human blood “spiked” with 5 or 10 cancer cells from different cell lines have been analyzed. Cancer cells were detected in all 571 cases. The sensitivity was found to be 90%. *IsoPic™ cell separation system.*



## Clinical validation

Prospective screening of 3388 individuals in a high-risk population (heredity, smoking, increased PSA, hepatitis B or C infection) in the ages of 45-80 with no symptoms or history of cancer.

### Results<sup>1</sup>

CTCs were found in 107 (3,2%) individuals which are now undergoing further evaluation.

## Medical laboratory accreditation

An application has been submitted for ISO 15189 accreditation (filed in January 2018).

## Product

The cell separation system *IsoPic™*, is CE-marked according to the ISO 13485 IVDD (In vitro diagnostic directive) and is patent protected.



*IsoPic™ cell separation system.*

## Clinical utility

### CUP (Cancer of Unknown Primary)

iCellate has entered a collaboration with RCC (Regionalt Cancer Centrum), tasked with improving and unifying care, to assist in diagnosing patients with suspected CUP. All patients with a suspected cancer will be screened for CTC and sequenced for determination of tumor location and possible treatment options.

### Heredity

Together with the heredity center at the New Karolinska Hospital (NKS), a targeted screening study is planned. iCellate will screen women with inherited BRCA- or TP53 mutations. In this study the utility of CTC is also evaluated and compared to ctDNA to determine the value of CTC for early detection of the clinical debut of the latent, inherited, disease.

### Prostate screening

The best current screening methods for prostate cancer are limited to the PSA-test (Prostate Specific Antigen) and lately with the additional tests included in the STHLM3-test. The PSA-test is notorious for over-diagnosing prostate cancer and triggering aggressive treatments that have serious side effects and carry large costs. In fact, it turns out in hindsight that only 25% of the individuals with a positive PSA finding had a tumor that needed treatment. This causes unnecessary medical procedures and anxiety. A prostate validation program is under development together with the Karolinska University Hospital.

### Pharma development

iCellate has developed the tools to be the perfect partner for new pharmacological development. By detection of CTC and the downstream analyses that the isolation of CTCs allows, iCellate can assist in matching patients with the right treatment option.

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<sup>1</sup> Under review for publication (Q1 2018).