

# Aristotle: A single blood test for pan-cancer screening.

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## Background

Blood participates in physiological and pathological changes throughout the body which are reflected as changes in cellular gene expression. The involvement of the immune system in cancer suppression and promotion through immunoediting exemplifies this. These characteristics make blood a promising non-invasive surrogate tissue for cancer diagnosis and monitoring.

## Methods

A multi-class cancer classification model, Aristotle, was developed with logistic regression using Affymetrix gene expression profiles generated from 2,845 unique human whole peripheral blood samples. The model was evaluated through 100 iterations of 2-fold cross-validation.

## Results

The 1,013 cancer patient samples (age  $61\pm 13$ , 40.6% ♀), include cancer of the bladder (n = 87, age  $65\pm 11$ , 23.3% ♀), breast (n = 94, age  $54\pm 10$ , 98.4% ♀), colon (n = 205, age  $64\pm 13$ , 39.5% ♀)/colon polyps (n = 226, age  $61\pm 11$ , 36.0% ♀), cervix (n = 36, age  $55\pm 13$ ), endometrium (n = 25, age  $49\pm 12$ ), liver (n = 16, age  $57\pm 11$ , 12.5% ♀), nasopharynx (n = 78, age  $51\pm 13$ , 26.9% ♀), ovaries (n = 64, age  $55\pm 12$ ), prostate (n = 160, age  $68\pm 9$ ) or stomach (n = 22, age  $59\pm 11$ , 28.6% ♀); and 1,832 control samples (age  $53\pm 16$ , 38.9% ♀), including healthy subjects (n = 1,042, age  $55\pm 16$ , 37.0% ♀) and subjects with ankylosing spondylitis (n = 59, age  $39\pm 12$ , 18.6% ♀), heart failure (n = 193, age  $67\pm 12$ , 40.0% ♀), inflammatory bowel disease (n = 51, age  $37\pm 9$ , 40.0% ♀), osteoarthritis (n = 248, age  $53\pm 15$ , 45.6% ♀), rheumatoid arthritis (n = 40, age  $57\pm 17$ , 84.6% ♀), schizophrenia (n = 110, age  $36\pm 13$ , 43.6% ♀) or other (n = 89, age  $50\pm 14$ , 41.1% ♀). Aristotle classified cancer profiles with sensitivities from 55.6-100% and positive predictive values from 5.6-77.7% at a specificity of 99.0% (Table). The mean false positive rate for the 11 cancer classes ranged from 0.3- 6.8%.

## Conclusions

Our study demonstrates the clinical viability of using whole peripheral blood for multi-class cancer classification. Aristotle was capable of classifying patients with different types of cancer with clinically relevant accuracy. We are confident that Aristotle holds great promise to help address the need for practical and non-invasive early-stage cancer diagnostics.

**Table. Classification Summary of the n=2,845 Cancer Samples**

	Bladder	Breast	Colon	Colon Polyps	Cervical	Endometrial	Liver	NPC	Ovarian	Prostate	Stomach
n	87	94	205	226	36	25	16	78	64	160	22
Sensitivity (%)*	90.8	87.2	55.6	59.3	100	96	93.8	100	92.2	72.5	100
Prevalence (%)^	0.31	3.85	0.69	7.58	0.22	0.81	0.06	0.22	0.23	3.76	0.07
PPV (%)	22.1	77.7	27.8	82.9	17.9	43.8	5.6	18.2	17.4	73.9	6.6
NPV (%)	100	99.5	99.7	96.7	100	100	100	100	100	98.9	100

\*at 99.0% Specificity; ^Ages 50 to 74