#1036

Detection of circulating tumor DNA by whole genome sequencing enables prediction of recurrence in stage III colorectal cancer patients with great inter-lab reproducibility

Amanda Frydendahl[1], Jesper Nors[1], Mads Heilskov[1], Ester Ellegaard Sørensen[1], Thomas Reinert[1], Jesper Bramsen[1], Danielle Afterman[3], Tomer Lauterman[3], Maja Kuzman[2], Santiago Gonzalez[2], Dunja Glavas[2], James Smadback[2], Dillon Maloney[2], Jurica Levativ[2], Sunil Deochand[2], Michael Yahalom[3], Ryan Ptashkin[2], Iman Tavassoly[2], Zohar Donenhirsh[3], Eric White[2], Ravi Kandasamy[2], Ury Alon[3], Paz Polak[2], Anders Husted Madsen[4], Uffe S. Løve[5], Per Vadgaard Andersen[6], Ole Thorlacius-Ussing[7], Lene Hjerrild Iversen[8], Kåre Andersson Gotschalck[9], Boris Oklander[3], Asaf Zviran[2], Claus Lindbjerg Andersen[1]

[1]Department of Molecular Medicine, Aarhus University Hospital, Denmark, [2]C2i Genomics Inc., New York, NY10014, USA, [3]C2i Genomics, Ltd., Haifa, Israel, [4]Department of Surgery, Herning Regional Hospital, [5]Department of Surgery, Viborg Regional Hospital, [6]Department of Surgery, Odense University Hospital, [7]Institute of Clinical Medicine, Aalborg University, [8]Department of Surgery, Aarhus University Hospital, [9]Department of Surgery, Horsens Regional Hospital

Amanda Frydendahl Johansen
amandafbj@clin.au.dk

Study summary

144 Stage III colorectal cancers

36 Recurrence cases

127 Recieved adjuvant chemotherapy

36 Months follow-up

144 Tumor samples

144 Germline samples

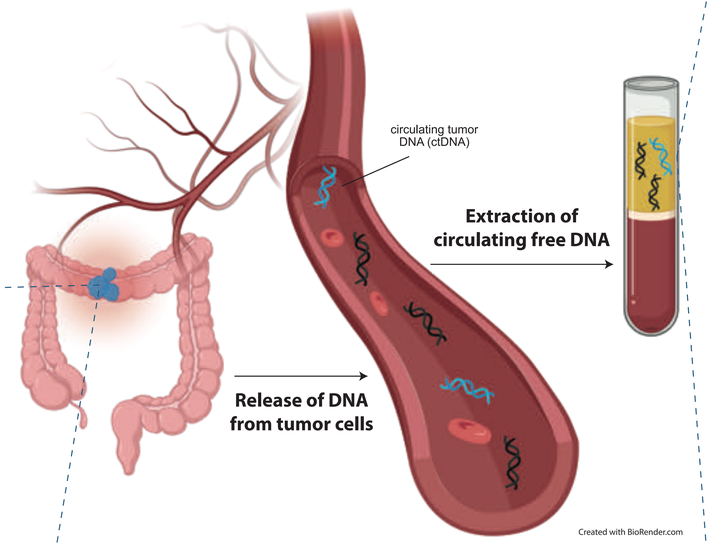
1283 Plasma samples

Whole-genome sequencing

Created with BioRender.com

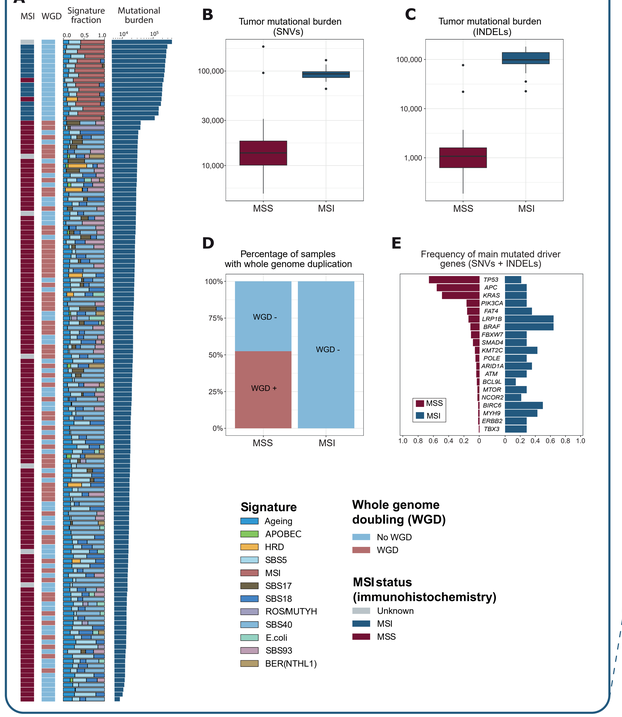
Key points

- Whole-genome sequencing at 20x coverage enables detection of circulating tumor DNA (ctDNA)
- Processing of paried samples in two independent laboratories shows great inter-lab reproducibility
- De-novo mutation calling of high-burden ctDNA samples identifies novel genomic alterations exclusive to plasma samples

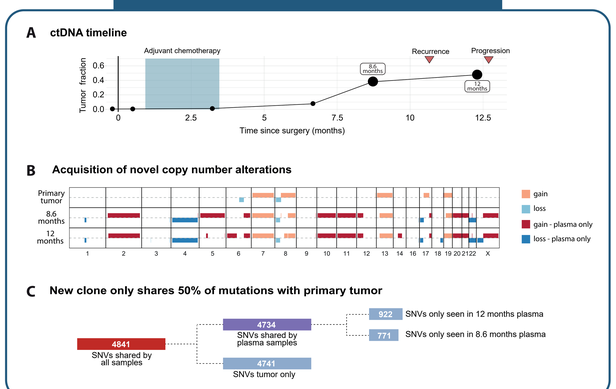


Created with BioRender.com

Tumor characteristics

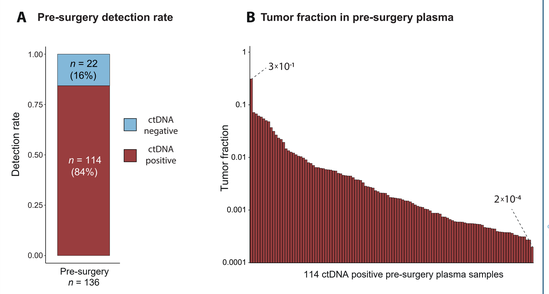


Novel changes in plasma



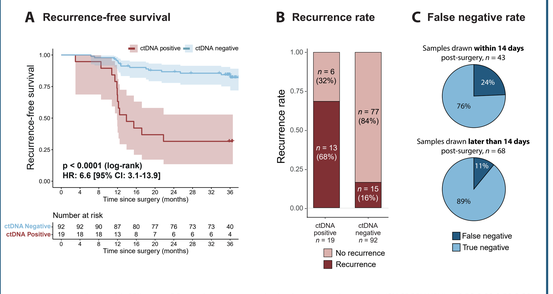
ctDNA results

Pre-surgery ctDNA detection



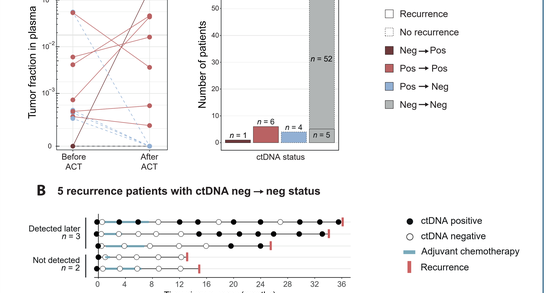
Post-surgery ctDNA detection*

* Plasma drawn within after surgery and before initiation of adjuvant chemotherapy



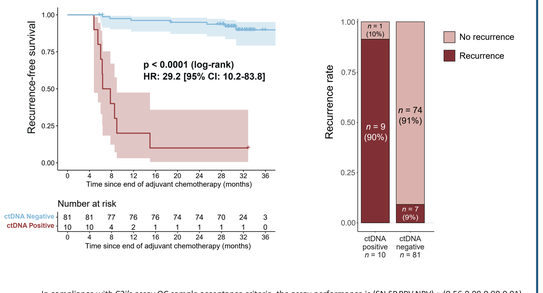
In compliance with C2i's assay QC sample acceptance criteria, the assay performance is (SN,SP,PPV,NPV) = (0.58,0.90,0.58,0.90)

Effect of adjuvant chemotherapy



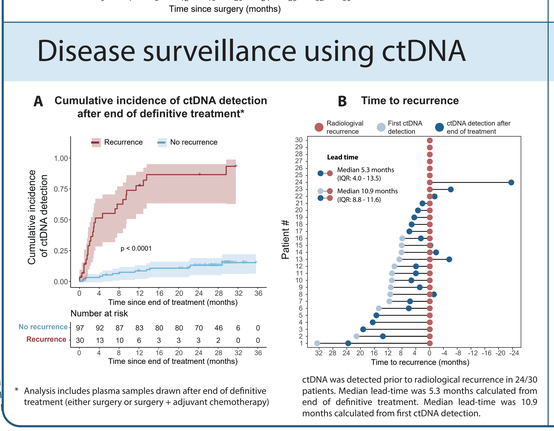
ctDNA post adjuvant chemotherapy*

* Plasma drawn within 3 months after end of adjuvant chemotherapy



In compliance with C2i's assay QC sample acceptance criteria, the assay performance is (SN,SP,PPV,NPV) = (0.56,0.99,0.90,0.91)

Disease surveillance using ctDNA



* Analysis includes plasma samples drawn after end of definitive treatment (either surgery or surgery + adjuvant chemotherapy)

ctDNA was detected prior to radiological recurrence in 24/30 patients. Median lead-time was 5.3 months calculated from end of definitive treatment. Median lead-time was 10.9 months calculated from first ctDNA detection.

Inter-lab reproducibility