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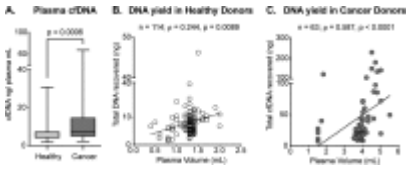

Fig. 1. Total cfDNA yield of plasma samples deriving from healthy donors or cancer patients.. From: Cell-free DNA analysis in healthy individuals by next-generation sequencing: a proof of concept and technical validation study.

a cfDNA concentration in plasma of healthy individuals compared to cancer patients (Mann–Whitney $p = 0.0006$). Median, interquartile range, and minimum/maximum are shown in the boxplot. **b** Correlation of plasma volume and the total cfDNA output in healthy donors ($n = 114$, Spearman $\rho = 0.244$, $p = 0.0089$). **c** Correlation between the plasma volume and the total cfDNA output in cancer patients ($n = 63$, Spearman $\rho = 0.587$, $p < 0.0001$)
Ilaria Alborelli, et al. Cell Death Dis. 2019 Jul;10(7):534.

CitationFull text

2.

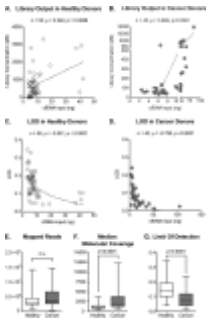

Fig. 2. Comparison of pre-analytical variables from healthy and cancer donor samples.. From: Cell-free DNA analysis in healthy individuals by next-generation sequencing: a proof of concept and technical validation study.

a, **b** Correlation of library concentration and input of cfDNA in healthy individuals ($n = 55$, Spearman $\rho = 0.348$, $p = 0.0088$) and cancer patients ($n = 40$, Spearman $\rho = 0.699$, $p < 0.0001$). **c**, **d** Correlation of LOD and cfDNA input in healthy ($n = 55$; Spearman $\rho = -0.551$, $p < 0.0001$) and cancer donors ($n = 40$; Spearman $\rho = -0.790$, $p < 0.0001$). **e** Mapped reads of samples deriving from healthy and cancer donors (Mann–Whitney $p = 0.1422$). **f**, **g** Median molecular coverage (Mann–Whitney $p < 0.0001$) and LOD (Mann–Whitney $p < 0.0001$) in healthy and cancer donors. Median, interquartile range, and minimum/maximum are shown in the boxplot
Ilaria Alborelli, et al. Cell Death Dis. 2019 Jul;10(7):534.

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3.

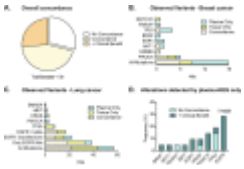

Fig. 3. Concordance analysis of liquid and tissue biopsy in cancer patients.. From: Cell-free DNA analysis in healthy individuals by next-generation sequencing: a proof of concept and technical validation study.

a Representation of the percentage of overall concordance of matched tissue and liquid biopsy. "+Clinical benefit" refers to additional clinically relevant mutations that were detected through NGS analysis of liquid biopsy and not tissue biopsy (see "plasma only" in the next sections). No concordance was observed in 29% of the samples, whereas out of 71% concordant samples 26% carried additional clinically relevant mutations detected by plasma only (+ Clinical Benefit). **b**, **c** Number of observed variants for breast (**b**) and lung (**c**) cancer samples. Only clinically relevant variants covered by both tissue and plasma NGS panels were considered for the analysis. **d** Distribution of gene alterations detected by NGS analysis of plasma and not detected in tissue (total $n = 24$). Among the clinically relevant mutations that were detected through NGS analysis of liquid biopsy and not tissue biopsy, the most frequent (32%) is T790M in EGFR. Mutations found by plasma alone were subdivided in the "+ Clinical Benefit" category if they were part of additionally clinically relevant mutations detected by plasma alone in samples showing overlap in tissue and plasma mutational profiles (i.e. concordance for oncogenic drivers). The "No Concordance" category indicates mutations detected in samples showing no overlap in tissue and plasma mutational profiles
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4.

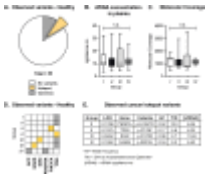

Fig. 4. Genetic alterations detected in the cfDNA of healthy individuals.. From: Cell-free DNA analysis in healthy individuals by next-generation sequencing: a proof of concept and technical validation study.

a No genetic alteration was detected in 84% of the assayed samples; however, we detected six germline and four hotspot variants in seven different samples. **b**, **c** Pre-analytical variables as cfDNA concentration in plasma (**b**) and median molecular coverage (**c**) in the four groups of healthy donors (Kruskal–Wallis $p = 0.9223$ and $p = 0.7721$, respectively). Group I: healthy at follow-up time; group II: benign breast condition at follow-up time; group III: breast cancer at follow-up time; group IV: a solid tumor other than breast cancer at follow-up time. Median, interquartile range, and minimum/maximum are shown in the boxplot. **d** Mutational matrix indicating the variants detected in healthy individuals belonging to the four groups. Each line represents a patient. Yellow squares represent hotspot variants; gray squares represent germline variants. **e** Table summarizing the hotspot variants detected in healthy individuals. LOD limit of detection, AF allele frequency; TtD Time to hyperplasia/cancer Detection, [cfDNA] cfDNA concentration in plasma (cfDNA ng/plasma ml)

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