













**Supplemental Table S6:** Starting plasma volume and SILAC standard amount in each experiment. Number of proteins reflects total identifications for the label-free experiments and total quantified proteins (with ratio values) for the SILAC experiments. <sup>a</sup> Average results.

Experiment	Tube	Plasma volume (ml)	SILAC standard protein amount (µg)	# proteins
Technical repeats, label free	Polycarbonate / polypropylene tubes suitable for Sorvall SS34 rotor (round bottom)	3	-	3, <b>2</b> 94 <sup>a</sup>
Standard comparison - CLMPs		3	6.7	1,992
Standard comparison - Lysate		3	6.7	2,473
Standard comparison - Secretome		3	6.7	910
Prostate cancer and healthy donors samples	Eppendorf LoBind microcentrifuge tubes	0.5	6	2,167ª

## Supplementary figure legends:

Supplemental FIG. S1. **Selected examples of tissue leakage proteins.** Average intensities and peptide numbers of selected proteins in triplicate runs of plasma microparticles (*A*), and in unfractionated plasma (*B*).

Supplemental FIG. S2. **Distribution of the ratios between plasma microparticles and the super-SILAC mix.** Core plasma proteins (from Fig. 1*B*) are colored in blue. *A.* Histograms of CLMP (cell line microparticles) super-SILAC standard. *B.* Histograms of lysate super-SILAC standard.

Supplemental FIG. S3. **Reproducibility of the super-SILAC standards.** Histograms of the coefficient of variation of three technical replicates of the ratio between plasma microparticles and the super SILAC mix.

Supplemental FIG. S4. Comparison between prostate cancer patients and healthy samples using PROMIS-Quan. Hierarchical clustering of significantly changing proteins between the two groups divided the signature into 2 clusters. One cluster includes 132 proteins that are higher in prostate cancer patients' plasma microparticles, and the second cluster includes 46 proteins that are lower in the same group. Patient samples are coded according to patient number and sample number (e.g., 'Patient1\_2' is patient 1 sample 2). Sample 1 = before radiation treatment; Sample 2 = 24 hours after first radiation treatment; Sample 3 = 2 weeks after first radiation treatment.

## Supplemental tables:

Supplementary Table S1. **Peptides of single-peptide proteins.** *A.* Plasma microparticles technical replicates and unfractionated plasma. *B.* Super-SILAC standard types. *C.* Super-SILAC triplicates. *D.* Prostate cancer patients samples compared to healthy donors samples. Values are in log2. Peptides that were identified only in reverse are marked and gray

Supplementary Table S2. **Peptide Tables.** *A.* Plasma microparticles technical replicates and unfractionated plasma. *B.* Super-SILAC standard types. *C.* Super-SILAC triplicates. *D.* Prostate cancer patients samples compared to healthy donors samples. Values are in log2.

Supplementary Table S3. **Protein Tables.** *A.* Plasma microparticles technical replicates and unfractionated plasma. *B.* Super-SILAC standard types. *C.* Super-SILAC triplicates. *D.* Prostate cancer patients samples compared to healthy donors samples. Values are in log2. Proteins that were identified only by site or in reverse are marked and gray (were not included in the analysis)

Supplementary Table S4. **Selected proteins and their average concentration.** Concentration values are based on downloaded data from PPD (calculated average).

Supplementary Table S5. Welch's t-test between healthy donors and prostate cancer patients. Patient samples are coded according to patient number and number of sample (e.g.,

'Patient1\_2' is patient 1 sample 2). Sample 1 = before radiation treatment; Sample 2 = 24 hours after first radiation treatment; Sample 3 = 2 weeks after first radiation treatment.

Supplemental Table S6: **Starting plasma volume and SILAC standard amount in each experiment.** Number of proteins reflects total identifications for the label-free experiments and total quantified proteins (with ratio values) for the SILAC experiments. <sup>a</sup> Average results.