OFF-CHIP SAMPLE PREPARATION			
CHEMICAL LYSIS			
Sample type	**Off-chip sample pretreatment**	**Lysis type**	**Reference**
Whole blood, 50 µL	Load solution preparation (50 µL): Sample (50 µL), 30% Triton X-100 (17 µL), Proteinase K (30 µL; at 20 mg/mL) and loading buffer (403 µL) containing 6M GuHCl, 10 mM Tris, 1 mM EDTA, pH 6.0. Mixing for 30 sec.	Chemical	33
Whole blood, 4 µL Nasal Aspirate, 8 µL	Load solution preparation (100 µL): Sample (4 or 8 µL), Proteinase K (5 µL), 6M GuHCl (91 or 87 µL). Vortexing for 30 sec.	Chemical	44
Semen, 1.5 µL	Load solution preparation (200 µL): Sample (1.5 µL), 6M GuHCl with 40mM DDT (198.5 µL). Vortexing.	Chemical	76
Whole blood, 4 µL Semen, 5 µL Buccal/nasal swab, 10 µL	Load solution preparation: Crude sample or cells in water solution (4/10/5/10 µL), Proteinase K (10/20/0/10 µL), GuHCl (486/500/495/180 µL) added of 40mM DDT in case of semen. Vortexing for 15 sec.	Chemical	25
Whole blood, 10 µL Spinal fluid, 40 µL	Load solution preparation (1000 µL): Sample (10 or 40 µL), 10% or 1% Triton X-100 (54 µL or 60 µL). Vortexing for 5 min. Reaching the final volume by addition of 6M GuHCl. Filtration with 0.22 µm sterile filter before loading.	Chemical	43
Whole blood, 50 µL	Load solution preparation: Sample (50 µL) pipetted for 5 min with GuSCN-based lysis buffer (RLT Buffer, Qiagen) at room temperature	Chemical	48
Whole blood, 20 µL	Load solution preparation (400 µL): Sample (20 µL); Proteinase K (20 µL),1% Triton X-100 (160 µL), NaCl and water (200 µL).	Chemical	37
Whole blood, 0.1 - 100 µL Throat swabs, 300 µL	Load solution preparation: Blood (0.1 to 100 µL) mixed with GuSCN-based lysis buffer (350 - 700 µL; Buffer RLT, Qiagen). Throat swabs solution (300 µL) mixed with lysis/binding buffer (350 µL; 100mM Tris-HCl, 500mM LiCl, 10mM EDTA, 1% LiDS, 5mM DDT). Load solution is prepared by addition of oligo-dT magnetic beads, mixed and incubated at room temperature for 5 min, before charging on syringe pumps.	Chemical	30
Whole blood	Load solution preparation: Whole blood, with cancer cells, mixed with GuSCN-based lysis buffer (Buffer RLT, Qiagen) and pressure-vacuum delivered across the membrane.	Chemical	47
Nasal wash, 30 µL	Load solution preparation: Sample (30 µL) homogenized by hand passage into a 25-gauge needle for 5 times. Infected sample is mixed with lysis/binding buffer (300 µL; 2M GuSCN, 25mM sodium citrate, pH 7, 50% ethanol) and silica coated magnetic beads (20 µL). Mixed for 5 min at room temperature.	Chemical	70
Nasal wash/swab, 100 µL	Load solution preparation: Sample (100 µL) mixed with lysis buffer (300 µL; 2M GuSCN). Lysed solution is added with a syringe pump.	Chemical	69
Semen, 25 µL	Load solution preparation: Sample (4 µL) is mixed with lysis buffer (96 µL; 6M GuHCl with 40mM DDT) and loaded onto the chip with a syringe pump.	Chemical	10
Whole Blood, 5 µL	Load solution preparation: Sample (5 µL) mixed with lysis buffer (45 µL; 50mM MES, 1% Triton X-100 and 2 mg/µL of Proteinase K) and incubated for 30 min at room temperature. Lysed solution (50 µL) loaded with a manual syringe.	Chemical	45
Whole Blood, 90 µL	Load solution preparation: sample (90 µL) is mixed with lysis buffer (GuSCN-based), detergents (N-lauroylsarcosine, 2-mercaptoethanol, NP-40) and incubated for 15 min at room temperature.	Chemical	40
MECHANICAL + CHEMICAL LYSIS			
Whole blood, 10 µL	DNA pre-concentration on lysate: lysis buffer (125 µL; 6M GuHCl) loaded onto the octadecyl (C18) reversed-phase pre-column. Sample (10 µL) is then loaded. DNA is pre-concentrated and eluted from this phase, which then binds proteins with stronger affinity than DNA, as a sieve.	Mechanical Chemical	38
Stool, 180-220 mg	Sample (180 - 220 mg) mixed and incubated with 5.5M GuSCN (700 µL) for 30 min. Lysed sample filtered on a 0.2 µm pore-size filter prior the extraction to ensure the correct fluid circulation and prevent a blockage by solid pieces. Liquid stool samples are well processed by this device without the use of electrical energy but, in case of solid stool samples, it would be necessary to centrifuge the sample before the use.	Mechanical Chemical	74

Table S1: Pretreatment procedures applied to different sample types when an off-chip lysis was performed prior the loading on LOC. Similarly to the described on-chip lysis procedures (Table2), guanidinium salts (GuHCl and GuSCN), often coupled with detergents, are the most used chaotropic agents with the capacity of solubilizing proteins.

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