CLAIMS

1. Method for detecting and quantifying at least one type of target molecules by quantifying molecules-molecules interactions, comprising:

(a) grafting unlabelled molecules on one or more array(s),

(b) labelling with different exogenous elements ~~one or more exogenous element(s) which are element(s) not naturally contained in the circulating or grafted molecules,~~ one or more type(s) of ~~circulating~~ molecules that are free in one or more solution(s),

wherein each of said different exogenous elements is an element, which is not naturally contained in said free molecules and which is not naturally contained in said grafted molecules, and

wherein each of said different exogenous elements is selected from the group of elements consisting of I, Br, F, S, Au, Fe, Se, As, P, B, Cu, Ag, Zn and Ni;

(c) placing said ~~putting~~ solution(s) ~~containing circulating molecule(s)~~ into contact with the one or more array(s) obtained from step (a), before or after the labelling step (b), under conditions that allow the unlabelled grafted molecules present on the array(s) to interact with the ~~circulating~~ molecules of said solution(s), ~~from the solution, ,~~

(d) washing and drying the array,

(e) ~~possibly~~ locating the so-obtained spots,

(f) detecting and counting by Dynamic Secondary Ion Mass Spectrometry (D-SIMS) said different exogenous elements ~~element(s)~~ or a group of elements containing said different exogenous elements ~~element(s)and possibly a reference natural element present on the spot for each spot of each array~~,

(g) calculating the ratio(s) between spots of the values of the counting by D-SIMS of each exogenous elements ~~element(s)~~ and/or calculating the ratio(s) ~~for each spot~~ between the value of the counting by D-SIMS of each exogenous elements ~~element(s) and the value of the counting by D-SIMS of a reference natural element present on the spot, for example in the grafted molecules or in the grafting buffer~~.

2. Method according to claim 1 ~~in two solutions of at least one type of molecules~~, comprising the following steps in this order:

(a) grafting unlabelled molecules on one or more array(s),

(b1) labelling with an exogenous element X at least one ~~a~~ type of ~~circulating~~ molecules that are free in a solution 1;

(b2) labelling with an exogenous element Y different from X at least one ~~a~~ type of ~~circulating~~ molecules that are free in a solution 2 different from 1;

(c) putting said solutions 1 and 2 into contact with an array under conditions that allow the unlabelled grafted molecules present on the array to interact with the ~~circulating~~ molecules of said solutions 1 and 2,

(d) washing and drying the array

(e) locating the so-obtained spots,

(f) detecting and counting by D-SIMS said exogenous elements X or a group of elements containing X and Y or a group of elements containing Y ~~and/or a reference natural element present on the spot~~ for each spot of each array.

(g) calculating the ratio(s) for each spot between the values of the counting by D-SIMS

- of exogenous elements X and Y of solutions 1 and 2~~,~~

~~and/or~~

~~- of the reference natural element present on the spot and the exogenous element X of solution 1~~

~~and/or~~

~~- of the reference natural element present on the spot and the exogenous element Y of solution 2~~.

3. Method according to claim 1 for detecting and quantifying in at least one solution of at least one type of ~~circulating~~ molecules, comprising the following steps in this order:

(a) grafting unlabelled molecules on one or more array(s),

(b1) labelling with an exogenous element X at least one ~~a~~ type of ~~circulating~~ molecules that are free in a part of a solution 1;

(b2) labelling with an exogenous element Y different from X the same type of ~~circulating~~ molecules that are free in a part of a solution 2 different from 1;

(c1) putting said X-labelled solution 1 and Y-labelled solution 2 into contact with an array 3 under conditions that allow the unlabelled grafted molecules present on the array to interact with the ~~circulating~~ molecules of said X-labelled solution 1 and of said Y-labelled solution 2,

(b3) labelling with an exogenous element Y at least one ~~a~~ type of ~~circulating~~ molecules that are free in a part of solution 1;

(b4) labelling with an exogenous element X the same type of ~~circulating~~ molecules that are free in a part of solution 2;

(c2) putting said Y-labelled solution 1 and X-labelled solution 2 into contact with an array 4 identical with array 3 under conditions that allow the unlabelled grafted molecules present on the array to interact with the ~~circulating~~ molecules of said Y-labelled solution 1 and of said X-labelled solution 2,

(d) washing and drying the arrays 3 and 4

(e) locating the so-obtained spots,

(f1) detecting and counting by D-SIMS said exogenous elements X or a group of elements containing X and Y or a group of elements containing Y for each spot of the array 3

(f2) detecting and counting by D-SIMS said exogenous elements X or a group of elements containing X and Y or a group of elements containing Y for each spot of the array 4

(g1) calculating the ratios X/Y for each spot between the values of the counting by D-SIMS of exogenous elements X and Y for array 3

(g2) calculating the ratios X/Y for each spot between the values of the counting by D-SIMS of exogenous elements X and Y for array 4

(h) comparing for each spot the results of the ratios obtained in steps (g1) and (g2).

4. Method according to claim 1 ~~in two solutions of at least one type of molecules~~, comprising the following steps in this order:

(a) grafting unlabelled molecules on one or more array(s),

(b1) adding an exogenous element X to at least one ~~a~~ type of molecules in a solution 1;

(b2) adding ~~with~~ an exogenous element Y different from X to the same type of molecules in a solution 1;

(c1) putting said X-labelled solution 1 and Y-labelled solution 1 into contact with an array 3 under conditions that allow the unlabelled grafted molecules present on the array to interact with the ~~circulating~~ molecules of said X-labelled solution 1 and Y-labelled solution 1,

(b3) adding the an exogenous element Y to at least one ~~a~~ type of molecules in a solution 2;

(c2) putting said X-labelled solution 1 and Y-labelled solution 2 into contact with an array 4 identical with array 3 under conditions that allow the unlabelled grafted molecules present on the array to interact with the ~~circulating~~ molecules of said X-labelled solution 1 and Y-labelled solution,

(d) washing and drying the arrays 3 and 4,

(e) locating the so-obtained spots,

(f1) detecting and counting by D-SIMS said exogenous elements X or a group of elements containing X and Y or a group of elements containing Y for each spot of the array 3,

(f2) detecting and counting by D-SIMS said exogenous elements X or a group of elements containing X and Y or a group of elements containing Y for each spot of the array 4,

(g1) calculating the ratios X/Y for each spot between the values of the counting by D-SIMS of exogenous elements X and Y for array 3

(g2) calculating the ratios X/Y for each spot between the values of the counting by D-SIMS of exogenous elements X and Y for array 4

(h) comparing for each spot the results of the ratios obtained in steps (g1) and (g2).

5. Method according to claim 1 for detecting at least one post-translational modification in a protein, comprising the following steps in this order:

(a) grafting unlabelled molecules on one or more array(s),

(b1) labelling with an exogenous element X proteins in a sampled solution 1;

(b2) labelling with an exogenous element Y different from X proteins in a sampled solution 1;

(c1) putting said X-labelled solution 1 and Y-labelled solution 1 into contact with an array 3 under conditions that allow the unlabelled grafted molecules present on the array to interact with the target proteins,

(c'1) putting into contact with array 3 an antibody or a lectin specific to the post-translational modification to be detected, said antibody or lectin being labelled with an exogenous element Z

(b3) labelling with an exogenous element Y proteins in a solution 2;

(c2) putting said X-labelled solution 1 and Y-labelled solution 2 into contact with an array 4 identical with array 3 under conditions that allow the unlabelled grafted molecules present on the array to interact with the target proteins,

(c'2) putting into contact with array 4 an antibody or lectin specific to the post-translational modification to be detected, said antibody or lectin being labelled with an exogenous element Z

(d) washing and drying the arrays 3 and 4

(e) locating the so-obtained spots,

(f1) detecting and counting by D-SIMS said exogenous element X or a group of elements containing X and Y or a group of elements containing Y and Z or a group of elements containing Z for each spot of the array 3

(f2) detecting and counting by D-SIMS said exogenous elements X or a group of elements containing X and Y or a group of elements containing Y and Z or a group of elements containing Z for each spot of the array 4

(g1) calculating the ratios X/Y, X/Z and Y/Z for each spot between the values of the counting by D-SIMS of exogenous elements X, Y and Z for array 3

(g2) calculating the ratios X/Y, X/Z and Y/Z for each spot between the values of the counting by D-SIMS of exogenous elements X, Y and Z for array 4

(h) comparing for each spot the results of the ratios obtained in steps (g1) and (g2).

6. Method according to claim 1 ~~for several solutions using several circulating probes~~ comprising the following steps in this order:

(a) spotting unlabelled molecules on one or more array(s),

(b1) labelling with an exogenous element X at least one ~~a~~ type of ~~circulating~~ molecules

(b2) labelling with an exogenous element Y different from X another type of ~~circulating~~ molecules

(b3) labelling with an exogenous element Z different from X and Y another type of ~~circulating~~ molecules

(c1) placing ~~putting~~ said X-labelled, Y-labelled and Z-labelled ~~circulating~~ molecules free in a solution,

(c2) putting said X, Y and Z labelled molecules ~~probes solutions~~ into contact with an array made of sampled molecules grafted on the support on spots, at least one spot for each sample to be tested, under conditions that allow the unlabelled sampled molecules grafted on the array to interact with said X-labelled, Y-labelled and Z-labelled molecules, ~~the circulating labelled probes,~~

(d) washing and drying the array,

(e) locating the so-obtained spots,

(f) detecting and counting by D-SIMS said exogenous elements X or a group of elements containing X and said exogenous element Y or a group of elements containing Y and said exogenous element Z or a group of elements containing Z for each spot

(g) calculating the ratios X/Y, X/Z and Y/Z for each spot between the values of the counting by D-SIMS of exogenous elements X, Y and Z.

7. Method according to any of the preceding claims, wherein the molecules grafted in step (a) are the probes and wherein said one or more type(s) of molecules, which are free in one or more solution(s) and which are labelled with different exogenous elements, ~~the circulating molecules of step (c)~~ are the target molecules.

8. Method according to any of the preceding claims, wherein the molecules grafted in step(a) are the target molecules to be tested and wherein said one or more type(s) of molecules, which are free in one or more solution(s) and which are labelled with different exogenous elements, ~~the circulating molecules of step (c)~~ are the probes.

~~9.Method according to any of the preceding claims, wherein said exogenous elements are selected in the group consisting of I, Br, F, S, Au, Fe, Se, As, P, B, Cu, Ag, Zn, Ni.~~

9. ~~10.~~ Method according to any of the preceding claims, wherein said different exogenous elements are selected from ~~the circulating molecules are labelled by an exogenous element selected in~~ the group of elements consisting of I, Br, F.

10. ~~11.~~ Method according to any of the preceding claims, wherein said target molecule(s) is(are) in a sample, which has been previously isolated from ~~the samples to be tested may be isolated from~~ cells, tissue, organ, body fluid, ~~such as for instance~~ sera, plasma, seminal fluid, synovial fluid, cerebrospinal fluid, blood or urine, a cell culture, a cell lysate, water, ~~such as~~ sewage water, freshwater, marine coastal water, ground water or any solution containing biomolecules.

11. Method according to any of the preceding claims, wherein said target molecules comprise nucleic acids, oligonucleotides, DNA, RNA, PNA, aptamers, peptides, proteins, antibodies, enzymes, lectins, an antigen, enzyme substrate, receptor or ligand for the receptor, glycans, lipids, polyamines, phages, viruses or a combination thereof.

~~12. Method according to any of the preceding claims, wherein the molecules to be tested may comprise nucleic acids, peptides or proteins, lectins, ligands, glycans, lipids, polyamines. phages, viruses or a combination thereof.~~

12. Method according to any of the preceding claims, wherein said target molecules comprise peptide or proteins.

13. Method ~~of proteomic or genomic research~~ according to any of the preceding claims, wherein ~~several samples in the form of solution are screened in order to measure individual variations.~~ said target molecules are detected and quantified to determine individual variations in proteomic or genomic research analysis, for predicting a predisposition to a disease, for diagnosing a disease, or for screening therapeutic agents.

14. Method of diagnosis according to any of the preceding claims, wherein at least one solution is a reference sample and at least one solution is a ~~potentially pathological~~ sample containing biomolecules from cells, tissue, organ or body fluid.

15. Kit for diagnosis or proteomic or genomic research comprising array(s), probes and exogenous elements suitable for carrying out the method according to any of the preceding claims.

16. The kit of claim 15, wherein said kit comprises
array(s),

unlabelled molecules, which are grafted onto said array(s), and

one or more type(s) of molecules, which are labelled with different exogenous elements, and which is(are) bound to said grafted unlabelled molecules,

wherein each of said different exogenous elements is an element, which is not naturally contained in said molecules and which is not naturally contained in said grafted molecules, and

wherein each of said different exogenous elements is selected from the group of elements consisting of I, Br, F, S, Au, Fe, Se, As, P, B, Cu, Ag, Zn and Ni.