

Press, N.Y. for a more detailed description of other antibody fragments). While various antibody fragments are defined in terms of the digestion of an intact antibody, one of skill will appreciate that such fragments may be synthesized de novo either chemically, by utilizing recombinant DNA methodology, or by "phage display" methods (see, e.g., Vaughan et al. (1996) *Nature Biotechnology*, 14(3): 309-314, and PCT/US96/10287). Preferred antibodies include single chain antibodies, e.g., single chain Fv (scFv) antibodies in which a variable heavy and a variable light chain are joined together (directly or through a peptide linker) to form a continuous polypeptide. As specific non-limiting examples, the antibody may be murine (e.g., Orthoclone OKT3, etc.), chimeric (e.g., Rituximab, Remicade, etc.), humanized (e.g., Avastin, Herceptin, etc.), human (e.g., Humira, etc.). In some cases, the species comprises a monoclonal antibody, a domain antibody, an antibody fragment (e.g., scFv, Fv, Fab, etc.), or the like.

[0051] Various embodiments herein are described with reference to antibodies. However, it should be understood that in some cases, such descriptions also include, as other embodiments, fragments or portions of antibodies. For example, a cell may be contained within a droplet that is able to express a portion of an antibody, for example, a light chain or a heavy chain of an antibody, a fragment of an antibody, etc.

[0052] In some cases, the antibody may be one that is selected to have certain desired characteristics, such as the ability to bind to a particular protein (e.g., with a relatively high binding affinity), or even to a particular epitope. For instance, an antibody may bind to a first portion of the protein but not a second portion of the protein, or the antibody may bind to a first protein but not bind to a second protein. In some cases, the second protein may be substantially similar to the first protein, i.e., the antibody may display relatively high specificity to the first protein. Thus, for example, the affinity of the antibody for an antigen or a cell (e.g., relative affinities between different antibodies, absolute affinity, etc.), the off-rate of the antibody from its antigen, the activity of an antibody, and/or the performance of antibodies and/or antibody fragments relative to known therapeutic agents may all be determined in various embodiments.

[0053] The cell secreting or producing the antibody (i.e., the antibody-producing cell) may be an immortal or a non-immortal cell. In one embodiment, the antibody-producing cell is a hybridoma cell. For instance, a hybridoma cells are often produced by fusing a non-immortal antibody-producing cell, such as a B-cell, with a tumor cell such as a myeloma tumor cell. The hybridoma cell thus has been genetically engineered or altered. In some cases, however, a non-immortal antibody-producing cell may be desirable. The cell may be one that arises from a subject (e.g., a human), and/or one that has been cultured. The non-immortal antibody-producing cell may be one that is able to produce antibodies under naturally occurring conditions, and often produces "normal" or properly-folded antibodies, even when inside a fluidic droplet as discussed herein.

[0054] However, it should be understood that the invention is not limited to only antibody-producing cells. Other cells, e.g., able to secrete a species of interest are contemplated in other embodiments as well. For instance, the cell may secrete a hormone such as insulin (secreted by beta cells), a neurotransmitter such as dopamine or serotonin, a protein or a peptide such as ACTH (adrenocorticotrophic hormone) or angiotensin, a messenger such as NO, or the like. As mentioned, the cell may be one that naturally secretes such spe-

cies, or a cell genetically engineered to secrete the species. For instance, the cell may be a genetically engineered bacteria, such as *E. coli*.

[0055] In some aspects, the fluidic droplets may each be substantially the same shape and/or size ("monodisperse"). For example, the fluidic droplets may have a distribution of dimensions such that no more than about 10% of the fluidic droplets have a dimension greater than about 10% of the average dimension of the fluidic droplets, and in some cases, such that no more than about 8%, about 5%, about 3%, about 1%, about 0.3%, about 0.1%, about 0.03%, or about 0.01% have a dimension greater than about 10% of the average dimension of the fluidic droplets. In some cases, no more than about 5% of the fluidic droplets have a dimension greater than about 5%, about 3%, about 1%, about 0.3%, about 0.1%, about 0.03%, or about 0.01% of the average dimension of the fluidic droplets.

[0056] The shape and/or size of the fluidic droplets can be determined, for example, by measuring the average diameter or other characteristic dimension of the droplets. The term "determining," as used herein, generally refers to the analysis or measurement of a species, for example, quantitatively or qualitatively, and/or the detection of the presence or absence of the species. "Determining" may also refer to the analysis or measurement of an interaction between two or more species, for example, quantitatively or qualitatively, or by detecting the presence or absence of the interaction. Examples of suitable techniques include, but are not limited to, spectroscopy such as infrared, absorption, fluorescence, UV/visible, FTIR ("Fourier Transform Infrared Spectroscopy"), or Raman; gravimetric techniques; ellipsometry; piezoelectric measurements; immunoassays; electrochemical measurements; optical measurements such as optical density measurements; circular dichroism; light scattering measurements such as quasioelectric light scattering; polarimetry; refractometry; or turbidity measurements.

[0057] The "average diameter" of a plurality or series of droplets is the arithmetic average of the average diameters of each of the droplets. Those of ordinary skill in the art will be able to determine the average diameter (or other characteristic dimension) of a plurality or series of droplets or particles, for example, using laser light scattering, microscopic examination, or other known techniques. The diameter of a droplet, in a non-spherical droplet, is the diameter of a perfect sphere having the same volume as the droplet. The average diameter of a droplet may be, for example, less than about 1 mm, less than about 500 micrometers, less than about 200 micrometers, less than about 100 micrometers, less than about 75 micrometers, less than about 50 micrometers, less than about 40 micrometers, less than about 25 micrometers, less than about 10 micrometers, less than about 5 micrometers, less than about 1 micrometer, less than about 0.3 micrometers, less than about 0.1 micrometers, less than about 0.03 micrometers, or less than about 0.01 micrometers in some cases. The average diameter of the droplet(s) may also be at least about 1 micrometer, at least about 2 micrometers, at least about 3 micrometers, at least about 5 micrometers, at least about 10 micrometers, at least about 15 micrometers, or at least about 20 micrometers in certain cases. The volume may be determined, for example, by impedance measurement, optical techniques (for example a fluorophore of known concentration could be added to the drop-forming media and total amount of that fluorophore could be measured in each drop as an index of volume), microscopy, or the like.