WHAT IS CLAIMED IS:

1. A method of localizing a macromolecule at a target tissue or cell of a subject, the method comprising administering to the subject a macromolecule comprising a first binding site and a second binding site, wherein:

(a) the first binding site is specific for an effector target in the subject, and

(b) the second binding site is specific for an address target expressed in the target tissue or cell in the subject;

wherein:

(i) the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell;

(ii) the second binding site does not substantially influence signaling upon binding the address target; and

(iii) the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site; and

allowing the macromolecule to localize at the target tissue or cell of the subject.

2. The method of claim 1, wherein at least 25% of the macromolecule detectable in the subject is detected at the target tissue or cell at a time point between 1 and 7 days following administration of the macromolecule to the subject.

3. The method of claim 1, wherein the potency of the first binding site at the target tissue or cell is substantially increased relative to a reference macromolecule lacking the second binding site, optionally wherein the first binding site has a low affinity for the effector target or a low avidity for the effector target.

4. The method of claim 1, wherein a) the affinity of the first binding site for the effector target is lower than the affinity of the second binding site for the address target or b) the avidity of the first binding site for the effector target is lower than the avidity of the second binding site for the address target.

5. The method of claim 1, wherein effector target signaling by the macromolecule in a non-target tissue or cell of the subject is substantially decreased relative to a reference macromolecule lacking the second binding site.

6. The method of claim 1, wherein the address target is regionally expressed in the subject

7. The method of claim 1, wherein the address target is locally expressed in the subject.

8. The method of claim 1, wherein the expression of the address target is restricted to a cell type in the subject.

9. The method of claim 1, wherein the address target is expressed only by a cell in the subject when in a specific cell state.

10. The method of claim 1, wherein the address target is expressed only by a cell in the subject in a disease state.

11. The method of claim 1, wherein the first binding site or the second binding site comprises a polypeptide, optionally wherein the polypeptide is an antibody or antigen-binding fragment thereof.

12. The method of claim 11, wherein the macromolecule is an antibody comprising a first binding site that is specific for the effector target in the subject and a second binding site that is specific for the address target.

13. The method of claim 11, wherein the polypeptide is a ligand of the effector target or a ligand of the address target.

14. The method of claim 13, wherein:

(a) the first binding site comprises an antibody or antigen-binding fragment thereof and the second binding site comprises a ligand of the address target; or

(b) the first binding site comprises a ligand of the effector target and the second binding site comprises an antibody or antigen-binding fragment thereof.

15. The method of claim 1, wherein:

a) the target tissue is skin and the second binding site is specific for desmoglein-1 (DSG-1), or

b) the target tissue is lung tissue and the second binding site is specific for RAGE; or

c) the target tissue is kidney tissue and the second binding site is specific for cadherin 16 (CDH16); or

d) the target tissue is intestine tissue and the second binding site is specific for cadherin 17 (CDH17).