SUMMARY

[0011a] In one aspect, there is provided a composition comprising: (a) a plurality of intact, bacterially derived minicells, each minicell of the plurality encompassing regulatory RNA that is packaged in the minicell, and (b) a pharmaceutically acceptable carrier therefor, wherein (i) the regulatory RNA is selected from the group consisting of antisense ssRNA, ribozyme and decoy RNA, (ii) there is an absence from the minicells of a construct for *in situ* expression of the regulatory RNA, and (iii) the plurality comprises a therapeutically effective amount of the regulatory RNA.

[0012] In accordance with one embodiment of the disclosure, therefore, a composition comprising (a) a plurality of intact minicells, each minicell of the plurality encompassing plasmid-free functional nucleic acid, and (b) a pharmaceutically acceptable carrier therefor. The category of "functional nucleic acid" is illustrated by single-, double-, or multi-stranded DNA or RNA. In one embodiment, minicells of the plurality contain plasmid-free functional nucleic acid that is regulatory RNA. Examples of such regulatory RNA include, but are not limited to,siRNA, miRNA, and shRNA.

[0013] The minicell-packaged functional nucleic acid may target the RNA transcripts encoding a protein that contributes to drug resistance, to apoptosis resistance, or to neoplasticity, *inter alia*. Also, a composition of the disclosure may further comprise a bispecific ligand comprised, for example, of a first arm specific for a minicell surface structure and a second arm specific for a non-phagocytic mammalian cell surface receptor.

[0013a] In one aspect, there is provided an *in vitro* method of delivering regulatory RNA, comprising the steps of: (a) providing a plurality of intact, bacterially derived minicells in a pharmaceutically acceptable carrier, each minicell of the plurality encompassing regulatory RNA; and (b) bringing minicells of the plurality into *in vitro* contact with mammalian cells such that the mammalian cells engulf minicells of the plurality, whereby the regulatory RNA is released into the cytoplasm of the target cells, wherein (i) the regulatory RNA is selected from the group consisting of antisense ssRNA, ribozyme and decoy RNA, (ii) there is an absence from the minicells of a construct for in situ expression of the regulatory RNA, and (iii) the plurality comprises a therapeutically effective amount of the regulatory RNA.

[0013b] In one aspect, there is provided use of a composition as defined herein for the preparation of a medicament for *in vivo* delivery of regulatory RNA.

9. The composition of claim 1, wherein the composition comprises fewer than about 1 contaminating parent bacterial cell per 10^{10} minicells.

10. The composition of claim 1, wherein the composition comprises fewer than about 1 contaminating parent bacterial cell per 10^{11} minicells.

11. The composition of claim 1, wherein the regulatory RNA is antisense ssRNA.

12. An *in vitro* method of delivering regulatory RNA, comprising the steps of:

(a) providing a plurality of intact, bacterially derived minicells in a pharmaceutically acceptable carrier, each minicell of the plurality encompassing regulatory RNA; and

(b) bringing minicells of the plurality into *in vitro* contact with mammalian cells such that the mammalian cells engulf minicells of the plurality, whereby the regulatory RNA is released into the cytoplasm of the target cells,

wherein (i) the regulatory RNA is selected from the group consisting of antisense ssRNA, ribozyme and decoy RNA, (ii) there is an absence from the minicells of a construct for *in situ* expression of the regulatory RNA, and (iii) the plurality comprises a therapeutically effective amount of the regulatory RNA.

13. The use of a composition of claim 1 for the preparation of a medicament for *in vivo* delivery of regulatory RNA.

14. The use of claim 13, wherein said regulatory RNA is antisense ssRNA.

15. A method for formulating the composition of claim 1, comprising co-incubating a plurality of intact, bacterially derived minicells and the regulatory RNA in a buffer.

16. The method of claim 15, wherein said regulatory RNA is antisense ssRNA.