CLAIMS

WHAT IS CLAIMED IS:

1. ~~A method of treating a serrated tumor in a subject, comprising:~~ ~~administering to the subject~~ Use of a therapeutically effective amount of an inhibitor of hyaluronan activity or expression in the manufacture of a medicament for treating a serrated tumor in a subject, wherein a biological sample from the subject has lower levels of expression of PKCζ and PKC ƛ/ι compared to levels of expression of PKCζ and PKC ƛ/ι in an individual without a serrated tumor.

2. The use~~method~~ of claim 2, wherein the inhibitor of hyaluronan activity or expression comprises a small molecule, an inhibitor of hyaluronan-CD44 binding or agonism, or an antagonist of CD44 which is optionally an antibody inhibitor of CD44 activity or expression, or a small molecule inhibitor of CD44 activity or expression.

~~3. The method of any one of claims 1-2, wherein the inhibitor of hyaluronan activity or expression comprises an inhibitor of hyaluronan-CD44 binding or agonism.~~

~~4. The method of any one of claims 1-3, wherein the inhibitor of hyaluronan activity or expression comprises an antagonist of CD44.~~

~~5. The method of claim 4, wherein the inhibitor of hyaluronan activity or expression comprises an antibody inhibitor of CD44 activity or expression.~~

~~6. The method of claim 4, the inhibitor of hyaluronan activity or expression comprises a small molecule inhibitor of CD44 activity or expression.~~

~~7~~3. The use~~method~~ of ~~any one of claims 1-6~~claim 1 or 2, wherein the inhibitor of hyaluronan activity or expression comprises an agonist of hyaluronidase activity

or expression which is optionally exogenous hyaluronidase, recombinant hyaluronidase or Pegvorhyaluronidase alfa (PVHA).

~~8. The method of claim 7, wherein the inhibitor of hyaluronan activity or expression comprises exogenous hyaluronidase.~~

~~9. The method of claim 7, wherein the inhibitor of hyaluronan activity or expression comprises recombinant hyaluronidase.~~

~~10. The method of claim 7, wherein the inhibitor of hyaluronan activity or expression comprises Pegvorhyaluronidase alfa (PVHA).~~

~~11~~4. The use~~method~~ of claim ~~10~~3, where the therapeutically effective amount of the PVHA is between 0.01 to 0.5 mg/kg or between 0.02 to 0.4 mg/kg.

~~12. The method of any one of claims 10-11, where the therapeutically effective amount of the PVHA is between 0.02 to 0.4 mg/kg.~~

~~13~~5. The use~~method~~ of ~~claims 10-12~~claim 3 or 4, wherein the Pegvorhyaluronidase alfa (PVHA) is to be administered to the subject as a monotherapy.

~~14~~6. The use~~method~~ of any one of claims ~~1-13~~1 to 5, wherein the therapeutically effective amount of the inhibitor of hyaluronan activity or expression is sufficient to reduce tumorigenesis at least 30% in the subject compared to an untreated individual wherein optionally the tumorigenesis is quantified by counting serrated polyps and carcinomas.

~~15. The method of claim 14, wherein the tumorigenesis is quantified using by counting serrated polyps and carcinomas.~~

~~16~~7. The use~~method~~ of any one of claims ~~1-15~~1 to 6, wherein the therapeutically effective amount of the inhibitor of hyaluronan activity or expression is sufficient to reduce tumor burden at least 20% in the subject compared to an untreated individual wherein optionally the tumor burden is quantified using at least one of total number of tumors, average size of tumors, or tumor load.

~~17. The method of claim 16, wherein the tumor burden is quantified using at least one of total number of tumors, average size of tumors, or tumor load.~~

~~18~~8. The use~~method~~ of any one of claims ~~1-17~~1 to 7, wherein the therapeutically effective amount of the inhibitor of hyaluronan activity or expression is sufficient to reduce hyaluronan deposition in the tumor or wherein the therapeutically effective amount of the inhibitor of hyaluronan activity or expression is sufficient to reduce collagen deposition in the tumor or wherein optionally the biological sample comprises blood, blood plasma, sera, or tissue biopsy or wherein the low levels of expression of PKCζ and PKC ƛ/ι comprises low transcription level, low translation level, or low activity level of PKCζ and PKC ƛ/ι.

~~19. The method of any one of claims 1-18, wherein the therapeutically effective amount of the inhibitor of hyaluronan activity or expression is sufficient to reduce collagen deposition in the tumor.~~

~~20. The method of any one of claims 1-19, wherein the biological sample comprises blood, blood plasma, sera, or tissue biopsy.~~

~~21. The method of any one of claims 1-20, wherein the low levels of expression of PKCζ and PKC ƛ/ι comprises low transcription level, low translation level, or low activity level of PKCζ and PKC ƛ/ι.~~

~~22~~9. ~~A method of treating a serrated tumor in a subject, comprising:~~

~~administering to the subject~~Use of a therapeutically effective amount of an inhibitor of hyaluronan activity or expression in the manufacture of a medicament for treating a serrated tumor in a subject.

~~23~~10. The use~~method~~ of claim ~~22~~9, wherein the inhibitor of hyaluronan activity or expression comprises Pegvorhyaluronidase alfa (PVHA) wherein optionally the Pegvorhyaluronidase alfa (PVHA) is to be administered to the subject as a monotherapy.

~~24. The method of claim 23, wherein the Pegvorhyaluronidase alfa (PVHA) is administered to the subject as a monotherapy.~~

~~25~~11. The use~~method~~ of ~~any one of claims 23-24~~claim 10, where the therapeutically effective amount of the PVHA is between 0.01 to 0.5 mg/kg or between 0.02 to 0.4 mg/kg.

~~26. The method of any one of claims 23-25, where the therapeutically effective amount of the PVHA is between 0.02 to 0.4 mg/kg.~~

~~27~~12. The use~~method~~ of any one of claims ~~23-26~~9 to 11, the therapeutically effective amount of the inhibitor of hyaluronan activity or expression is sufficient to reduce tumorigenesis at least 30% in the subject compared to an untreated individual and/or wherein a biological sample from the subject has a lower levels of expression of PKCζ and PKC ƛ/ι compared to levels of expression of PKCζ and PKC ƛ/ι in an individual without a serrated tumor and optionally wherein the tumorigenesis is quantified by counting serrated polyps and carcinomas.

~~28. The method of any one of claims 22-27, wherein a biological sample from the subject has a lower levels of expression of PKCζ and PKC ƛ/ι compared to levels of expression of PKCζ and PKC ƛ/ι in an individual without a serrated tumor.~~

~~29. The method of any one of claims 22-28, wherein the therapeutically effective amount of the inhibitor of hyaluronan activity or expression is sufficient to reduce tumorigenesis at least 30% in the subject compared to an untreated individual.~~

~~30. The method of claim 29, wherein the tumorigenesis is quantified using by counting serrated polyps and carcinomas.~~

~~31~~13. The use~~method~~ of any one of claims ~~22-30~~9 to 12, wherein the therapeutically effective amount of the inhibitor of hyaluronan activity or expression is sufficient to reduce tumor burden at least 20% in the subject compared to an untreated individual wherein optionally the tumor burden is quantified using at least one of total number of tumors, average size of tumors, or tumor load.

~~32. The method of claim 31, wherein the tumor burden is quantified using at least one of total number of tumors, average size of tumors, or tumor load.~~

~~33~~14. The use~~method~~ of any one of claims ~~22-32~~9 to 13, wherein the therapeutically effective amount of the inhibitor of hyaluronan activity or expression is sufficient to reduce hyaluronan deposition in the tumor or wherein the therapeutically effective amount of the inhibitor of hyaluronan activity or expression is sufficient to reduce collagen deposition in the tumor.

~~34. The method of any one of claims 22-33, wherein the therapeutically effective amount of the inhibitor of hyaluronan activity or expression is sufficient to reduce collagen deposition in the tumor.~~

~~35~~15. The use~~method~~ of any one of claims ~~28-34~~9 to 14, wherein the biological sample comprises blood, blood plasma, sera, or tissue biopsy.