mechanisms that regulate the Snail superfamily of transcription factors is important.

There is therefore a need to establish a relationship between ZO-2 and the Snail superfamily of transcription factors and uses for such a relationship.

## Summary

In a ~~first~~one aspect, there is provided a method of identifying candidate agents capable of modulating interaction between a first polypeptide and a second polypeptide, wherein the first polypeptide is ZO-2/TJP2 or a functional variant thereof and the second polypeptide is a Snail zinc finger transcription factor family member or a functional variant thereof, the method comprising: a. contacting the first polypeptide with the second polypeptide and a candidate agent; and b. determining whether: i. the binding of the first polypeptide with the second polypeptide is decreased or increased in the presence of said candidate agent when compared with a control; or ii. whether the affinity, extent or amount of the binding between the first polypeptide and the second polypeptide is decreased or increased in the presence of said candidate agent when compared with a control.

In one aspect, there is provided an *in vitro* method of predicting the likelihood of tumor metastasis development or the effectiveness of a cancer treatment, the method comprising determining a change in the binding of a first polypeptide with a second polypeptide when compared with a control;

wherein the first polypeptide is ZO-2/TJP2 or a functional variant thereof and the second polypeptide is a Snail zinc finger transcription factor family member or a functional variant thereof.

In a ~~second aspect~~one example, there is provided a method of predicting the likelihood of tumor metastasis development or the effectiveness of a cancer treatment, the method comprising determining a change in: a. the binding of a first polypeptide with a second polypeptide when compared with a control; or b. the affinity, extent or amount of the binding between a first polypeptide and a second polypeptide when compared with a control; wherein the first polypeptide is ZO-2/TJP2 or a functional variant

thereof and the second polypeptide is a Snail zinc finger transcription factor family member or a functional variant thereof.

In ~~a third aspect~~yet another, there is provided a kit for identifying candidate agents capable of modulating the interaction between a first polypeptide and a second polypeptide, wherein the first polypeptide is ZO-2/TJP2 or a functional variant thereof and the second polypeptide is a Snail zinc finger transcription factor family member or a functional variant thereof, the kit comprising the first polypeptide, the second polypeptide and at least one candidate agent.

In one aspect, there is disclosed herein use of an agent, which decreases the binding of a first polypeptide and a second polypeptide, wherein the first polypeptide is ZO-2/TJP2 or a functional variant thereof and the second polypeptide is a Snail zinc finger transcription factor family member or a functional variant thereof, in the manufacture of a medicament for treating, inhibiting or suppressing tumor growth

In another aspect, there is disclosed herein use of an agent which decreases the binding of a first polypeptide and a second polypeptide, wherein the first polypeptide is ZO-2/TJP2 or a functional variant thereof and the second polypeptide is a Snail zinc finger transcription factor family member or a functional variant thereof in the manufacture of a medicament for inhibiting tumor metastasis.

In yet another aspect, there is disclosed herein use of an agent which increases the binding of a first polypeptide and a second polypeptide, wherein the first polypeptide is ZO-2/TJP2 or a functional variant thereof and the second polypeptide is a Snail zinc finger transcription factor family member or a functional variant thereof in the manufacture of a medicament for enhancing wound healing.

In ~~a fourth aspect~~one example, there is provided a method of treating, inhibiting or suppressing tumor growth comprising: administering an agent which decreases the binding of a first polypeptide and a second polypeptide, wherein the first polypeptide is ZO-2/TJP2 or a functional variant thereof and the second polypeptide is a Snail zinc finger transcription factor family member or a functional variant thereof.

In ~~a fifth aspect~~another example, there is provided a method of inhibiting tumor metastasis comprising: administering an agent which decreases the binding of a first polypeptide and a second polypeptide, wherein the first polypeptide is ZO-2/TJP2 or a functional variant thereof and the second polypeptide is a Snail zinc finger transcription factor family member or a functional variant thereof.

In ~~a sixth aspect~~yet another example, there is provided a method of enhancing wound healing comprising: administering an agent which increases the binding of a first polypeptide and a second polypeptide, wherein the first polypeptide is ZO-2/TJP2 or a functional variant thereof and the

second polypeptide is a Snail zinc finger transcription factor family member or a functional variant thereof.

In ~~a seventh~~one aspect, there is provided an isolated complex between ZO-2/TJP2 and a Snail zinc finger transcription factor family member.

In ~~an eighth~~another aspect, there is provided the use of the isolated complex as defined herein as a biomarker for detecting cancer.

In ~~a ninth~~yet another aspect, there is provided an antibody directed against the binding portion of ZO-2/TJP2 and SNAI2 (Slug) at the guanylate kinase (GUK) domain of ZO-2/TJP2.

**Detailed Description**

It has now been discovered that nuclear ZO-2 directly interacts with the Snail superfamily of zinc finger transcription factors. In particular, the interaction of ZO-2 with a Snail zinc finger transcription factor enhances the nuclear retention of the ZO-2/Snail complex and hence protection from proteasomal degradation. It has been found that during early stages of epithelial-to-mesenchymal transition (EMT), nuclear translocation of ZO-2 may sequester Slug into the nucleus, which would then trigger a full or partial EMT to enhance migratory properties of cells by down-regulating epithelial markers. As it has been found that Slug and SNAI1 (Snail) were capable of down-regulating many epithelial markers, the entry of ZO-2 into the nucleus may serve to feed-forward a positive feedback loop that favored the initiation of a full or partial EMT.

that the candidate agent is useful for enhancing wound healing.

11. The method of any one of the preceding claims, wherein a change in the binding is determined by a method selected from the group consisting of a yeast two-hybrid system, a glutathione S-transferase (GST) binding assay, immunoprecipitation, immunofluorescence and combinations thereof.

12. An *in vitro* method of predicting the likelihood of tumor metastasis development or the effectiveness of a cancer treatment, the method comprising determining a change in the binding of a first polypeptide with a second polypeptide when compared with a control;
wherein the first polypeptide is ZO-2/TJP2 or a functional variant thereof and the second polypeptide is a Snail zinc finger transcription factor family member or a functional variant thereof.

13. The method of claim 12, wherein a decrease in the binding of the first polypeptide and the second polypeptide indicates a decrease in tumor metastasis development or an increase in effectiveness in cancer treatment.

14. The method of any one of claims 12 or 13, wherein the method is selected from the group consisting of a yeast two-hybrid system, a glutathione S-transferase (GST) binding assay, immunoprecipitation, immunofluorescence and combinations thereof.

15. A kit for identifying candidate agents capable of modulating the interaction between a first polypeptide and a second polypeptide, wherein the first polypeptide is ZO-2/TJP2 or a functional variant thereof and the second polypeptide is a Snail zinc finger transcription factor family member or a functional variant thereof, the kit comprising the first polypeptide, the second polypeptide and at least one candidate agent.

16. Use of an agent, which decreases the binding of a first polypeptide and a second polypeptide, wherein the first polypeptide is ZO-2/TJP2 or a functional variant thereof and the second polypeptide is a Snail zinc finger transcription factor family member or a functional variant thereof, in the manufacture of a medicament for~~A method of~~ treating, inhibiting or suppressing tumor growth ~~comprising: administering an agent which decreases the binding of a first polypeptide and a second polypeptide, wherein the first polypeptide is ZO-2/TJP2 or a functional variant thereof and the second polypeptide is a Snail zinc finger transcription factor family member or a functional variant thereof~~.

17. Use of an agent which decreases the binding of a first polypeptide and a second polypeptide, wherein the first polypeptide is ZO-2/TJP2 or a functional variant thereof and the second polypeptide is a Snail zinc finger transcription factor family member or a functional variant thereof in the manufacture of a medicament for~~A method of~~ inhibiting tumor metastasis ~~comprising: administering an agent which decreases the binding of a first polypeptide and a second polypeptide, wherein the first polypeptide is ZO-2/TJP2 or a functional variant thereof and the second polypeptide is a Snail zinc finger transcription factor family member or a functional variant thereof~~.

18. Use of an agent which increases the binding of a first polypeptide and a second polypeptide, wherein the first polypeptide is ZO-2/TJP2 or a functional variant thereof and the second polypeptide is a Snail zinc finger transcription factor family member or a functional variant thereof in the manufacture of a medicament for~~A method of~~ enhancing wound healing ~~comprising: administering an agent which increases the binding of a first polypeptide and a second polypeptide, wherein the first polypeptide is ZO-2/TJP2 or a functional variant thereof and the second~~

~~polypeptide is a Snail zinc finger transcription factor family member or a functional variant thereof~~.

19. An isolated complex between ZO-2/TJP2 and a Snail zinc finger transcription factor family member.

20. The complex of claim 19, wherein the Snail zinc finger transcription factor family member is SNAI2 (Slug).

21. The complex of claim 20, wherein the binding portion of ZO-2/TJP2 and SNAI2 (Slug) is at the guanylate kinase (GUK) domain of ZO-2/TJP2.

22. The complex of claim 21, wherein the guanylate kinase (GUK) domain of ZO-2/TJP2 comprises SEQ ID NO: 26.

23. Use of the isolated complex of any one of claims 19-22 as a biomarker for detecting cancer.

24. An antibody directed against the binding portion of ZO-2/TJP2 and SNAI2 (Slug) at the guanylate kinase (GUK) domain of ZO-2/TJP2.

25. The antibody of claim 24, wherein the guanylate kinase (GUK) domain of ZO-2/TJP2 comprises SEQ ID NO: 26.