

CLAIMS

1. A method for determining a circulating TGF β level in a blood sample or sample derived therefrom, comprising:
 - (a) processing the blood sample or sample derived from blood at a temperature of 2-8 °C in a sample tube comprising an anticoagulant, wherein the anticoagulant comprises a citrate-theophylline-adenosine-dipyridamole (CTAD) solution;
 - (b) carrying out one or more centrifugation steps; and/or carrying out a centrifugation protocol comprising a first centrifugation and a second centrifugation; and
 - (c) measuring a level of platelet factor 4 (PF4) in the blood sample or sample derived therefrom.
2. The method of claim 1, wherein the one or more centrifugation steps are carried out at a speed of greater than 100xg or below 15000xg.
3. The method of claim 1 or 2, wherein the first centrifugation of step (b) is slower than the second centrifugation.
4. The method of any of claims 1-3, wherein the first and second centrifugations of step (b) comprise:
 - (i) 10 minutes at 150xg and 20 minutes at 2500xg;
 - (ii) 10 minutes at 2500xg and 20 minutes at 2500xg; or
 - (iii) 10 minutes at 1500xg and 5 minutes at 12000xg.
5. The method of any of claims 1-4, wherein the anticoagulant comprises 0.11 M buffered trisodium citrate solution, 15 M theophylline, 3.7 M adenosine, and 0.198 M dipyridamole, and wherein the anticoagulant has a pH of about 5.0.
6. The method of any of claims 1-5, wherein the sample is used for determining a circulating TGF β level only if the PF4 level in the sample is less than 500 ng/ml.

7. The method of any of claims 1-6, wherein the circulating TGF β is circulating latent TGF β 1.
8. Use of a TGF β inhibitor in the manufacture of a medicament for the treatment of cancer in a subject, comprising:
 - (i) determining a level of circulating TGF β in a blood sample from the subject according to the method of any of claims 1-7;
 - (ii) administering to the subject the medicament comprising a therapeutically effective dose of a TGF β inhibitor;
 - (iii) determining a further level of circulating TGF β in a blood sample from the subject; and
 - (iv) administering the medicament comprising a further therapeutically effective dose of the TGF β inhibitor if the level of circulating TGF β in step (iii) is increased as compared to the level of circulating TGF β in step (i);wherein the increase is at least 1.5-fold.
9. The use of claim 8, further comprising administering a checkpoint inhibitor and/or a genotoxic therapy.
10. The use of claim 9, wherein the checkpoint inhibitor is an anti-PD-1 antibody, an anti-PD-L1 antibody, an anti-CTLA-4-antibody, an anti-LAG3 antibody, or an antigen-binding fragment thereof; and wherein the genotoxic therapy is a chemotherapy or a radiation therapy.
11. The use of claim 10, wherein the chemotherapy is a PARP inhibitor therapy.
12. The use of any of claims 8-11, wherein the subject has an advanced cancer and/or a solid cancer.
13. The use of claim 12, wherein the advanced cancer and/or the solid cancer is selected from melanoma, breast cancer, colorectal cancer, lung cancer, esophageal cancer, pancreatic cancer, bladder cancer, kidney cancer, uterine cancer, stomach cancer, head and neck cancer, urothelial carcinoma,

hepatocellular carcinoma, thyroid cancer, and tenosynovial giant cell tumor (TGCT).

14. The use of claim 13, wherein the melanoma is metastatic melanoma; the renal cell carcinoma, the breast cancer is triple-negative breast cancer or HER2-positive breast cancer; the colorectal cancer is microsatellite stable-colorectal cancer or colon adenocarcinoma; the lung cancer is metastatic non-small cell lung cancer or small cell lung cancer; the kidney cancer is transitional cell carcinoma, renal sarcoma, or renal cell carcinoma (RCC); the uterine cancer is uterine corpus endometrial carcinoma or prostate cancer; the stomach cancer is gastric cancer; and the head and neck cancer is head and neck squamous cell cancer; and
wherein the RCC is clear cell RCC, papillary RCC, chromophobe RCC, collecting duct RCC, or unclassified RCC.
15. Use of a TGF β inhibitor in the manufacture of a medicament for the treatment of a proliferative disorder in a subject, comprising:
 - (i) determining a level of P-Smad2 nuclear translocation in a biopsy sample from the subject;
 - (ii) administering to the subject the medicament comprising a therapeutically effective dose of a TGF β inhibitor;
 - (iii) further determining a level of the P-Smad2 nuclear translocation in a biopsy sample from the subject; and
 - (iv) administering the medicament comprising a further therapeutically effective dose of the TGF β inhibitor if the further determined level of P-Smad2 nuclear translocation of step (iii) is decreased compared to the level of P-Smad2 determined in step (i);wherein the decrease is at least 1.3-fold.
16. The use of 15, wherein the level of P-Smad2 nuclear translocation is determined by immunohistochemistry and nuclear masking analysis.

17. A method for identifying an mMDSC population and a gMDSC population from a biological sample obtained from a subject comprising detection of cell surface markers comprising:
- (i) applying a CD15⁺/CD66b^{high} filter; and
 - (ii) applying a CD15⁺/CD66b^{high}/CD14⁻/CD33^{low}/HLADR⁻/CD11b⁺ filter;
- wherein the mMDSC population is identified by the cell surface markers of CD11b⁺, HLA-DR⁻/low, CD14⁺, CD15⁻, CD33⁺/high, and CD66b⁻; and wherein the gMDSC population is identified by the cell surface markers of CD11b⁺, HLA-DR⁻, CD14⁻, CD15⁺, CD33⁺/low, and CD66b⁺.