WHAT IS CLAIMED IS:

1. A cell culture comprising human cells wherein at least about 5% of said human cells are preprimitive streak cells, said preprimitive streak cells being multipotent cells that can differentiate into mesendoderm cells.

2. The cell culture of claim 1, wherein at least about 10% of said human cells are preprimitive streak cells.

3. The cell culture of claim 1, wherein at least about 20% of said human cells are preprimitive streak cells.

4. The cell culture of claim 1, wherein at least about 30% of said human cells are preprimitive streak cells.

5. The cell culture of claim 1, wherein at least about 40% of said human cells are preprimitive streak cells.

6. The cell culture of claim 1, wherein at least about 50% of said human cells are preprimitive streak cells.

7. The cell culture of claim 1, wherein at least about 60% of said human cells are preprimitive streak cells.

8. The cell culture of claim 1, wherein at least about 70% of said human cells are preprimitive streak cells.

9. The cell culture of claim 1, wherein at least about 80% of said human cells are preprimitive streak cells.

10. The cell culture of claim 1, wherein at least about 90% of said human cells are preprimitive streak cells.

11. The cell culture of claim 1, wherein human feeder cells are present in said culture, and wherein at least about 5% of human cells other than said human feeder cells are preprimitive streak cells.

12. The cell culture of claim 1, wherein human feeder cells are present in said culture, and wherein at least about 25% of human cells other than said human feeder cells are preprimitive streak cells.

13. The cell culture of claim 1, wherein human feeder cells are present in said culture, and wherein at least about 50% of human cells other than said human feeder cells are preprimitive streak cells.

14. The cell culture of claim 1, wherein human feeder cells are present in said culture, and wherein at least about 75% of human cells other than said human feeder cells are preprimitive streak cells.

15. The cell culture of claim 1, wherein said primitive streak cells express a marker selected from the group consisting of FGF8 and nuclear-localized β-catenin.

16. The cell culture of claim 15, wherein the expression of a marker selected from the group consisting of FGF8 and nuclear-localized β-catenin is greater than the expression of a marker selected from the group consisting of brachyury, FGF4, SNAI1, SOX17, FOXA2, SOX7 and SOX1 in said preprimitive streak cells.

17. The cell culture of claim 15, wherein said preprimitive streak cells do not substantially express a marker selected from the group consisting of brachyury, FGF4, SNAI1, SOX17, FOXA2, SOX7 and SOX1.

18. The cell culture of claim 1, wherein said preprimitive streak cells express FGF8 and nuclear-localized β-catenin.

19. The cell culture of claim 18, wherein the expression of FGF8 and nuclear-localized β-catenin is greater than the expression of brachyury, FGF4, SNAI1, SOX17, FOXA2, SOX7 and SOX1 in said preprimitive streak cells.

20. The cell culture of claim 18, wherein said preprimitive streak cells do not substantially express brachyury, FGF4, SNAI1, SOX17, FOXA2, SOX7 and SOX1.

21. The cell culture of claim 1, wherein said cell culture is substantially free of cells selected from the group consisting of visceral endodermal cells, parietal endodermal cells, primitive endodermal cells, definitive endodermal cells, ectodermal cells and mesodermal cells.

22. The cell culture of claim 1 further comprising human embryonic stem cells (hESCs).

23. The cell culture of claim 22, wherein at least about 2 preprimitive streak cells are present for about every 1 hESC in said cell culture.

24. The cell culture of claim 22, wherein at least about 10 preprimitive streak cells are present for about every 1 hESC in said cell culture.

25. The cell culture of claim 22, wherein said hESC is derived from a tissue selected from the group consisting of the morula, the inner cell mass (ICM) of an embryo and the gonadal ridges of an embryo.

26. The cell culture of claim 1 further comprising a medium that comprises less than about 2% (v/v) serum.

27. The cell culture of claim 1 further comprising a medium that comprises less than about 1% (v/v) serum.

28. The cell culture of claim 1 further comprising a medium that comprises less than about 0.5% (v/v) serum.

29. The cell culture of claim 1 further comprising a medium that comprises less than about 0.2% (v/v) serum.

30. The cell culture of claim 1 further comprising a medium that lacks serum or lacks serum replacement.

31. The cell culture of claim 1 further comprising a growth factor of the Nodal/Activin subgroup of the TGFβ superfamily.

32. The cell culture of claim 31, wherein said growth factor of the Nodal/Activin subgroup of the TGFβ superfamily comprises activin A.

33. A cell culture comprising human cells wherein at least about 5% of said human cells are mesendoderm cells, said mesendoderm cells being multipotent cells that can differentiate into mesoderm cells or definitive endoderm cells.

34. The cell culture of claim 33, wherein at least about 10% of said human cells are mesendoderm cells.

35. The cell culture of claim 33, wherein at least about 20% of said human cells are mesendoderm cells.

36. The cell culture of claim 33, wherein at least about 30% of said human cells are mesendoderm cells.

37. The cell culture of claim 33, wherein at least about 40% of said human cells are preprimitive streak cells.

38. The cell culture of claim 33, wherein at least about 50% of said human cells are mesendoderm cells.

39. The cell culture of claim 33, wherein at least about 60% of said human cells are mesendoderm cells.

40. The cell culture of claim 33, wherein at least about 70% of said human cells are mesendoderm cells.

41. The cell culture of claim 33, wherein at least about 80% of said human cells are mesendoderm cells.

42. The cell culture of claim 33, wherein at least about 90% of said human cells are mesendoderm cells.

43. The cell culture of claim 33, wherein human feeder cells are present in said culture, and wherein at least about 5% of human cells other than said human feeder cells are mesendoderm cells.

44. The cell culture of claim 33, wherein human feeder cells are present in said culture, and wherein at least about 25% of human cells other than said human feeder cells are mesendoderm cells.

45. The cell culture of claim 33, wherein human feeder cells are present in said culture, and wherein at least about 50% of human cells other than said human feeder cells are mesendoderm cells.

46. The cell culture of claim 33, wherein human feeder cells are present in said culture, and wherein at least about 75% of human cells other than said human feeder cells are mesendoderm cells.

47. The cell culture of claim 33, wherein said mesendoderm cells express a marker selected from the group consisting of brachyury, FGF4 and SNAI1.

48. The cell culture of claim 47, wherein the expression of a marker selected from the group consisting of brachyury, FGF4 and SNAI1 is greater than the expression of a marker selected from the group consisting of OCT4, SOX17, CXCR4, FOXA2, SOX7 and SOX1 in said mesendoderm cells.

49. The cell culture of claim 47, wherein said mesendoderm cells do not substantially express a marker selected from the group consisting of OCT4, SOX17, CXCR4, FOXA2, SOX7 and SOX1.

50. The cell culture of claim 33, wherein said mesendoderm cells express brachyury, FGF4 and SNAI1.

51. The cell culture of claim 51, wherein the expression of brachyury, FGF4 and SNAI1 is greater than the expression of OCT4, SOX17, CXCR4, FOXA2, SOX7 and SOX1 in said mesendoderm cells.

52. The cell culture of claim 51, wherein said mesendoderm cells do not substantially express OCT4, SOX17, CXCR4, FOXA2, SOX7 and SOX1.

53. The cell culture of claim 33, wherein said cell culture is substantially free of cells selected from the group consisting of visceral endodermal cells, parietal endodermal cells, primitive endodermal cells, definitive endodermal cells, ectodermal cells and mesodermal cells.

54. The cell culture of claim 33 further comprising human embryonic stem cells (hESCs).

55. The cell culture of claim 54, wherein at least about 2 mesendoderm cells are present for about every 1 hESC in said cell culture.

56. The cell culture of claim 54, wherein at least about 10 mesendoderm cells are present for about every 1 hESC in said cell culture.

57. The cell culture of claim 54, wherein said hESC is derived from a tissue selected from the group consisting of the morula, the inner cell mass (ICM) of an embryo and the gonadal ridges of an embryo.

58. The cell culture of claim 33 further comprising a medium that comprises less than about 2% (v/v) serum.

59. The cell culture of claim 33 further comprising a medium that comprises less than about 1% (v/v) serum.

60. The cell culture of claim 33 further comprising a medium that comprises less than about 0.5% (v/v) serum.

61. The cell culture of claim 33 further comprising a medium that comprises less than about 0.2% (v/v) serum.

62. The cell culture of claim 33 further comprising a medium that lacks serum or lacks serum replacement.

63. The cell culture of claim 33 further comprising a growth factor of the Nodal/Activin subgroup of the TGFβ superfamily.

64. The cell culture of claim 63, wherein said growth factor of the Nodal/Activin subgroup of the TGFβ superfamily comprises activin A.

65. A cell population comprising cells wherein at least about 90% of said cells are human preprimitive streak cells, said preprimitive streak cells being multipotent cells that can differentiate into mesendoderm cells.

66. The cell population of claim 65, wherein at least about 95% of said cells are human preprimitive streak cells.

67. The cell population of claim 65, wherein at least about 98% of said cells are human preprimitive streak cells.

68. The cell population of claim 65, wherein said human preprimitive streak cells express a marker selected from the group consisting of FGF8 and nuclear-localized β-catenin.

69. The cell population of claim 68, wherein the expression of a marker selected from the group consisting of FGF8 and nuclear-localized β-catenin is greater than the expression of a marker selected from the group consisting of brachyury, FGF4, SNAI1, SOX17, FOXA2, SOX7 and SOX1 in said human preprimitive streak cells.

70. The cell population of claim 68, wherein said human preprimitive streak cells do not substantially express a marker selected from the group consisting of brachyury, FGF4, SNAI1, SOX17, FOXA2, SOX7 and SOX1.

71. The cell population of claim 65, wherein said human preprimitive streak cells express FGF8 and nuclear-localized β-catenin.

72. The cell population of claim 71, wherein the expression of FGF8 and β-catenin is greater than the expression of brachyury, FGF4, SNAI1, SOX17, FOXA2, SOX7 and SOX1 in said human preprimitive streak cells.

73. The cell population of claim 71, wherein said human preprimitive streak cells do not substantially express brachyury, FGF4, SNAI1, SOX17, FOXA2, SOX7 and SOX1.

74. A cell population comprising cells wherein at least about 90% of said cells are human mesendoderm cells, said mesendoderm cells being multipotent cells that can differentiate into mesoderm cells or definitive endoderm cells.

75. The cell population of claim 74, wherein at least about 95% of said cells are human mesendoderm cells.

76. The cell population of claim 74, wherein at least about 98% of said cells are human mesendoderm cells.

77. The cell population of claim 74, wherein said human mesendoderm cells express a marker selected from the group consisting of brachyury, FGF4 and SNAI1.

78. The cell population of claim 77, wherein the expression of a marker selected from the group consisting of brachyury, FGF4 and SNAI1 is greater than the expression of a marker selected from the group consisting of OCT4, SOX17, CXCR4, FOXA2, SOX7 and SOX1 in said human mesendoderm cells.

79. The cell population of claim 77, wherein said human mesendoderm cells do not substantially express a marker selected from the group consisting of OCT4, SOX17, CXCR4, FOXA2, SOX7 and SOX1.

80. The cell population of claim 74, wherein said human mesendoderm cells express brachyury, FGF4 and SNAI1.

81. The cell population of claim 77, wherein the expression of brachyury, FGF4 and SNAI1 is greater than the expression of OCT4, SOX17, CXCR4, FOXA2, SOX7 and SOX1 in said human mesendoderm cells.

82. The cell population of claim 77, wherein said human mesendoderm cells do not substantially express OCT4, SOX17, CXCR4, FOXA2, SOX7 and SOX1.

83. A method of producing preprimitive streak cells, said method comprising the steps of obtaining a cell population comprising pluripotent human cells and differentiating said pluripotent human cells in a medium comprising less than about 2% serum and at least one growth factor of the TGFβ superfamily, wherein said growth factor is present in the medium in an amount sufficient to promote differentiation of at least a portion of said pluripotent cells to preprimitive streak cells, said preprimitive streak cells being multipotent cells that can differentiate into mesendoderm cells.

84. The method of claim 83 further comprising the step of allowing sufficient time for preprimitive streak cells to form, wherein said sufficient time for preprimitive streak cells to form has been determined by detecting the presence of preprimitive streak cells in said cell population.

85. The method of claim 84, wherein sufficient time is at least about 6 hours.

86. The method of claim 84, wherein detecting the presence of preprimitive streak cells in said cell population comprises detecting the expression of at least one marker selected from the group consisting of FGF8 and nuclear-localized β-catenin and at least one marker from the group consisting of brachyury, FGF4, SNAI1, SOX17, FOXA2, SOX7 and SOX1 in cells of said cell population, wherein the expression of a marker selected from the group consisting of FGF8 and nuclear-localized β-catenin is greater than the expression of a marker selected from the

group consisting of brachyury, FGF4, SNAI1, SOX17, FOXA2, SOX7 and SOX1 in said preprimitive streak cells.

87. The method of claim 86, wherein the expression of at least one of said markers is determined by quantitative polymerase chain reaction (Q-PCR).

88. The method of claim 86, wherein the expression of at least one of said markers is determined by immunocytochemistry.

89. The method of claim 83, wherein at least about 5% of said pluripotent human cells differentiate into preprimitive streak cells.

90. The method of claim 83, wherein at least about 10% of said pluripotent human cells differentiate into preprimitive streak cells.

91. The method of claim 83, wherein at least about 20% of said pluripotent human cells differentiate into preprimitive streak cells.

92. The method of claim 83, wherein at least about 30% of said pluripotent human cells differentiate into preprimitive streak cells.

93. The method of claim 83, wherein at least about 40% of said pluripotent human cells differentiate into preprimitive streak cells.

94. The method of claim 83, wherein at least about 50% of said pluripotent human cells differentiate into preprimitive streak cells.

95. The method of claim 83, wherein at least about 60% of said pluripotent human cells differentiate into preprimitive streak cells.

96. The method of claim 83, wherein at least about 70% of said pluripotent human cells differentiate into preprimitive streak cells.

97. The method of claim 83, wherein at least about 80% of said pluripotent human cells differentiate into preprimitive streak cells.

98. The method of claim 83, wherein at least about 90% of said pluripotent human cells differentiate into preprimitive streak cells.

99. The method of claim 83, wherein said at least one growth factor is of the Nodal/Activin subgroup of the TGFβ superfamily.

100. The method of claim 99, wherein said at least one growth factor of the Nodal/Activin subgroup of the TGFβ superfamily comprises activin A.

101. The method of claim 83, wherein said at least one growth factor is provided in a concentration of at least about 10 ng/ml.

102. The method of claim 83, wherein said at least one growth factor is provided in a concentration of at least about 100 ng/ml.

103. The method of claim 83, wherein said at least one growth factor is provided in a concentration of at least about 500 ng/ml.

104. The method of claim 83, wherein said at least one growth factor is provided in a concentration of at least about 1000 ng/ml.

105. The method of claim 83, wherein said at least one growth factor is withdrawn after about 6 hours.

106. The method of claim 83, wherein said at least one growth factor is withdrawn after about 12 hours.

107. The method of claim 83, wherein said at least one growth factor is withdrawn after about 18 hours.

108. The method of claim 83, wherein said cell population is differentiated in a medium comprising less than about 1% (v/v) serum.

109. The method of claim 83, wherein said cell population is differentiated in a medium comprising less than about 0.5% (v/v) serum.

110. The method of claim 83, wherein said cell population is differentiated in a medium comprising less than about 0.2% (v/v) serum.

111. The method of claim 83, wherein said cell population is differentiated in a medium comprising less than about 0.1% (v/v) serum.

112. The method of claim 83, wherein said cell population is differentiated in the absence of serum or the absence of serum replacement.

113. The method of claim 83, wherein said cell population is differentiated in a medium comprising about 0% (v/v) serum on about the first day after adding said at least one growth factor, about 0.2% (v/v) serum or less on about the second day after adding said at least one growth factor and about 2% (v/v) serum or less on about the third day after adding said at least one growth factor.

114. The method of claim 83, wherein said cell population is differentiated in low serum RPMI medium.

115. The method of claim 83, wherein said pluripotent human cells comprise human embryonic stem cells (hESCs).

116. The method of claim 115, wherein said human embryonic stem cells are derived from a tissue selected from the group consisting of the morula, the inner cell mass (ICM) of an embryo and the gonadal ridges of an embryo.

117. A preprimitive streak cell produced by the method of claim 83.

118. A method of producing mesendoderm cells, said method comprising the steps of obtaining a cell population comprising pluripotent human cells and differentiating said pluripotent human cells in a medium comprising less than about 2% serum and at least one growth factor of the TGFβ superfamily, wherein said growth factor is present in the medium in an amount sufficient to promote differentiation of at least a portion of said pluripotent cells to mesendoderm

cells, said mesendoderm cells being multipotent cells that can differentiate into mesendoderm cells.

119. The method of claim 118 further comprising the step of allowing sufficient time for mesendoderm cells to form, wherein said sufficient time for mesendoderm cells to form has been determined by detecting the presence of mesendoderm cells in said cell population.

120. The method of claim 119, wherein sufficient time is at least about 24 hours.

121. The method of claim 118, wherein detecting the presence of mesendoderm cells in said cell population comprises detecting the expression of at least one marker selected from the group consisting of brachyury, FGF4 and SNAI1 and at least one marker from the group consisting of OCT4, SOX17, CXCR4, FOXA2, SOX7 and SOX1 in cells of said cell population, wherein the expression of a marker selected from the group consisting of brachyury, FGF4 and SNAI1 is greater than the expression of a marker selected from the group consisting of OCT4, SOX17, CXCR4, FOXA2, SOX7 and SOX1 in said mesendoderm cells.

122. The method of claim 121, wherein the expression of at least one of said markers is determined by quantitative polymerase chain reaction (Q-PCR).

123. The method of claim 121, wherein the expression of at least one of said markers is determined by immunocytochemistry.

124. The method of claim 118, wherein at least about 5% of said pluripotent human cells differentiate into mesendoderm cells.

125. The method of claim 118, wherein at least about 10% of said pluripotent human cells differentiate into mesendoderm cells.

126. The method of claim 118, wherein at least about 20% of said pluripotent human cells differentiate into mesendoderm cells.

127. The method of claim 118, wherein at least about 30% of said pluripotent human cells differentiate into mesendoderm cells.

128. The method of claim 118, wherein at least about 40% of said pluripotent human cells differentiate into mesendoderm cells.

129. The method of claim 118, wherein at least about 50% of said pluripotent human cells differentiate into mesendoderm cells.

130. The method of claim 118, wherein at least about 60% of said pluripotent human cells differentiate into mesendoderm cells.

131. The method of claim 118, wherein at least about 70% of said pluripotent human cells differentiate into mesendoderm cells.

132. The method of claim 118, wherein at least about 80% of said pluripotent human cells differentiate into mesendoderm cells.

133. The method of claim 118, wherein at least about 90% of said pluripotent human cells differentiate into mesendoderm cells.

134. The method of claim 118, wherein said at least one growth factor is of the Nodal/Activin subgroup of the TGFβ superfamily.

135. The method of claim 134, wherein said at least one growth factor of the Nodal/Activin subgroup of the TGFβ superfamily comprises activin A.

136. The method of claim 118, wherein said at least one growth factor is provided in a concentration of at least about 10 ng/ml.

137. The method of claim 118, wherein said at least one growth factor is provided in a concentration of at least about 100 ng/ml.

138. The method of claim 118, wherein said at least one growth factor is provided in a concentration of at least about 500 ng/ml.

139. The method of claim 118, wherein said at least one growth factor is provided in a concentration of at least about 1000 ng/ml.

140. The method of claim 118, wherein said at least one growth factor is withdrawn after about 24 hours.

141. The method of claim 118, wherein said at least one growth factor is withdrawn after about 36 hours.

142. The method of claim 118, wherein said at least one growth factor is withdrawn after about 48 hours.

143. The method of claim 118, wherein said cell population is differentiated in a medium comprising less than about 1% (v/v) serum.

144. The method of claim 118, wherein said cell population is differentiated in a medium comprising less than about 0.5% (v/v) serum.

145. The method of claim 118, wherein said cell population is differentiated in a medium comprising less than about 0.2% (v/v) serum.

146. The method of claim 118, wherein said cell population is differentiated in a medium comprising less than about 0.1% (v/v) serum.

147. The method of claim 118, wherein said cell population is differentiated in the absence of serum or the absence of serum replacement.

148. The method of claim 118, wherein said cell population is differentiated in a medium comprising about 0% (v/v) serum on about the first day after adding said at least one growth factor, about 0.2% (v/v) serum or less on about the second day after adding said at least one growth factor and about 2% (v/v) serum or less on about the third day after adding said at least one growth factor.

149. The method of claim 118, wherein said cell population is differentiated in low serum RPMI medium.

150. The method of claim 118, wherein said pluripotent human cells comprise human embryonic stem cells (hESCs).

151. The method of claim 150, wherein said human embryonic stem cells are derived from a tissue selected from the group consisting of the morula, the inner cell mass (ICM) of an embryo and the gonadal ridges of an embryo.

152. A mesendoderm cell produced by the method of claim 118.

153. A method of producing a cell population enriched in preprimitive streak cells, said method comprising the steps of obtaining a population of pluripotent cells, wherein at least one cell of said pluripotent cell population comprises at least one copy of a nucleic acid under the control of the FGF8 promoter, said nucleic acid comprising a sequence encoding green fluorescent protein (GFP) or a biologically active fragment thereof; differentiating said pluripotent cells so as to produce preprimitive streak cells, said preprimitive streak cells being multipotent cells that can differentiate into mesendoderm cells, and separating said preprimitive streak cells from cells which do not express GFP.

154. The method of claim 153, wherein said enriched cell population comprises at least about 95% preprimitive streak cells.

155. The method of claim 153, wherein said enriched cell population comprises at least about 98% preprimitive streak cells.

156. The method of claim 153, wherein the differentiating step comprises providing said pluripotent cell population with at least one growth factor from the TGFβ superfamily in an amount sufficient to promote differentiation of said pluripotent cells to preprimitive streak cells.

157. The method of claim 156, wherein said at least one growth factor of the TGFβ superfamily is activin A.

158. The method of claim 157, wherein said activin A is provided in a concentration of at least about 50 ng/ml.

159. The method of claim 157, wherein said activin A is provided in a concentration of at least about 100 ng/ml.

160. The method of claim 157, wherein said activin A is provided in a concentration of at least about 500 ng/ml.

161. The method of claim 153, wherein said cell population is differentiated in a medium comprising less than about 1% (v/v) serum.

162. The method of claim 153, wherein said cell population is differentiated in a medium comprising less than about 0.5% (v/v) serum.

163. The method of claim 153, wherein said cell population is differentiated in a medium comprising less than about 0.2% (v/v) serum.

164. The method of claim 153, wherein said cell population is differentiated in a medium comprising less than about 0.1% (v/v) serum.

165. The method of claim 153, wherein said cell population is differentiated in the absence of serum or the absence of serum replacement.

166. The method of claim 153, wherein said cell population is differentiated in a medium comprising about 0% (v/v) serum on about the first day after adding said at least one growth factor, about 0.2% (v/v) serum or less on about the second day after adding said at least one growth factor and about 2% (v/v) serum or less on about the third day after adding said at least one growth factor.

167. The method of claim 153, wherein said cell population is differentiated in low serum RPMI medium.

168. An enriched population of preprimitive streak cells produced by the method of claim 153.

169. A method of producing a cell population enriched in mesendoderm cells, said method comprising the steps of obtaining a population of pluripotent cells, wherein at least one cell of said pluripotent cell population comprises at least one copy of a nucleic acid under the control of a promoter selected from the group consisting of the brachyury promoter, the FGF4 promoter and the SNAI1 promoter, said nucleic acid comprising a sequence encoding green fluorescent protein (GFP) or a biologically active fragment thereof; differentiating said pluripotent cells so as to produce mesendoderm cells, said mesendoderm cells being multipotent cells that can differentiate into mesoderm cells or definitive endoderm cells, and separating said mesendoderm cells from cells which do not express GFP.

170. The method of claim 169, wherein said enriched cell population comprises at least about 95% mesendoderm cells.

171. The method of claim 169, wherein said enriched cell population comprises at least about 98% mesendoderm cells.

172. The method of claim 169, wherein the differentiating step comprises providing said pluripotent cell population with at least one growth factor of the TGFβ superfamily in an amount sufficient to promote differentiation of said pluripotent cells to mesendoderm cells.

173. The method of claim 172, wherein said at least one growth factor of the TGFβ superfamily is activin A.

174. The method of claim 173, wherein said activin A is provided in a concentration of at least about 50 ng/ml.

175. The method of claim 173, wherein said activin A is provided in a concentration of at least about 100 ng/ml.

176. The method of claim 173, wherein said activin A is provided in a concentration of at least about 500 ng/ml.

177. The method of claim 169, wherein said cell population is differentiated in a medium comprising less than about 1% (v/v) serum.

178. The method of claim 169, wherein said cell population is differentiated in a medium comprising less than about 0.5% (v/v) serum.

179. The method of claim 169, wherein said cell population is differentiated in a medium comprising less than about 0.2% (v/v) serum.

180. The method of claim 169, wherein said cell population is differentiated in a medium comprising less than about 0.1% (v/v) serum.

181. The method of claim 169, wherein said cell population is differentiated in the absence of serum or the absence of serum replacement.

182. The method of claim 169, wherein said cell population is differentiated in a medium comprising about 0% (v/v) serum on about the first day after adding said at least one growth factor, about 0.2% (v/v) serum or less on about the second day after adding said at least one growth factor and about 2% (v/v) serum or less on about the third day after adding said at least one growth factor.

183. The method of claim 169, wherein said cell population is differentiated in low serum RPMI medium.

184. An enriched population of mesendoderm cells produced by the method of claim 169.

185. A method of identifying a differentiation factor capable of promoting the differentiation of preprimitive streak cells in a cell population comprising human cells, said method comprising the steps of obtaining a cell population comprising human preprimitive streak cells, providing a candidate differentiation factor to said cell population, determining expression of a marker in said cell population at a first time point, determining expression of the same marker in said cell population at a second time point, wherein said second time point is subsequent to said first time point and wherein said second time point is subsequent to providing said population with said candidate differentiation factor, and determining if expression of the marker in said cell population at said second time point is increased or decreased as compared to the expression of the marker in said cell population at said first time point, wherein an increase or decrease in expression of said marker in said cell population indicates that said candidate differentiation factor is capable of promoting the differentiation of said preprimitive streak cells.

186. The method of claim 185, wherein said human preprimitive streak cells comprise at least about 10% of the human cells in said cell population.

187. The method of claim 185, wherein human feeder cells are present in said cell population and wherein at least about 10% of the human cells other than said feeder cells are preprimitive streak cells.

188. The method of claim 185, wherein said human preprimitive streak cells comprise at least about 50% of the human cells in said cell population.

189. The method of claim 185, wherein said human feeder cells are present in said cell population and wherein at least about 50% of the human cells other than said feeder cells are preprimitive streak cells.

190. The method of claim 185, wherein said human preprimitive streak cells differentiate into cells selected from the group consisting of mesendoderm, mesoderm and definitive endoderm in response to said candidate differentiation factor.

191. The method of claim 185, wherein said human preprimitive streak cells differentiate into mesendoderm cells in response to said candidate differentiation factor.

192. The method of claim 191, wherein said marker is selected from the group consisting of brachyury, FGF4 and SNAI1.

193. The method of claim 185, wherein said human preprimitive streak cells differentiate into mesoderm cells in response to said candidate differentiation factor.

194. The method of claim 193, wherein said marker is selected from the group consisting of FOXF1, FLK1, BMP4, MOX1 and SDF1.

195. The method of claim 185, wherein said human preprimitive streak cells differentiate into definitive endoderm cells in response to said candidate differentiation factor.

196. The method of claim 195, wherein said marker is selected from the group consisting of CXCR4 and SOX17.

197. The method of claim 185, wherein said first time point is prior to providing said candidate differentiation factor to said cell population.

198. The method of claim 185, wherein said first time point is at approximately the same time as providing said candidate differentiation factor to said cell population.

199. The method of claim 185, wherein said first time point is subsequent to providing said candidate differentiation factor to said cell population.

200. The method of claim 185, wherein expression of said marker is increased.

201. The method of claim 185, wherein expression of said marker is decreased.

202. The method of claim 185, wherein expression of said marker is determined by quantitative polymerase chain reaction (Q-PCR).

203. The method of claim 185, wherein expression of said marker is determined by immunocytochemistry.

204. The method of claim 185, wherein said candidate differentiation factor comprises at least one growth factor of the TGFβ superfamily.

205. The method of claim 204, wherein said at least one growth factor of the TGFβ superfamily is activin A.

206. The method of claim 185, wherein said candidate differentiation factor comprises a small molecule.

207. The method of claim 185, wherein said candidate differentiation factor comprises a polypeptide.

208. The method of claim 185, wherein said candidate differentiation factor is not a growth factor of the TGFβ superfamily.

209. The method of claim 185, wherein said candidate differentiation factor is provided to said cell population at a concentration of between about 0.1 ng/ml to about 10 mg/ml.

210. The method of claim 185, wherein said candidate differentiation factor is provided to said cell population at a concentration of between about 1 ng/ml to about 1 mg/ml

211. The method of claim 185, wherein said candidate differentiation factor is provided to said cell population at a concentration of between about 10 ng/ml to about 100 µg/ml.

212. The method of claim 185, wherein said candidate differentiation factor is provided to said cell population at a concentration of between about 100 ng/ml to about 10 µg/ml.

213. The method of claim 185, wherein said candidate differentiation factor is provided to said cell population at a concentration of about 1 µg/ml.

214. A method of identifying a differentiation factor capable of promoting the differentiation of mesendoderm cells in a cell population comprising human cells, said method comprising the steps of obtaining a cell population comprising human mesendoderm cells, providing a candidate differentiation factor to said cell population, determining expression of a marker in said cell population at a first time point, determining expression of the same marker in said cell population at a second time point, wherein said second time point is subsequent to said first time point and wherein said second time point is subsequent to providing said population with said candidate differentiation factor, and determining if expression of the marker in said cell population at said second time point is increased or decreased as compared to the expression of the marker in said cell population at said first time point, wherein an increase or decrease in expression of said marker in said cell population indicates that said candidate differentiation factor is capable of promoting the differentiation of said mesendoderm cells.

215. The method of claim 214, wherein said human mesendoderm cells comprise at least about 10% of the human cells in said cell population.

216. The method of claim 214, wherein human feeder cells are present in said cell population and wherein at least about 10% of the human cells other than said feeder cells are mesendoderm cells.

217. The method of claim 214, wherein said human mesendoderm cells comprise at least about 50% of the human cells in said cell population.

218. The method of claim 214, wherein said human feeder cells are present in said cell population and wherein at least about 50% of the human cells other than said feeder cells are mesendoderm cells.

219. The method of claim 214, wherein said human mesendoderm cells differentiate into cells selected from the group consisting of mesoderm and definitive endoderm in response to said candidate differentiation factor.

220. The method of claim 214, wherein said human mesendoderm cells differentiate into mesoderm cells in response to said candidate differentiation factor.

221. The method of claim 220, wherein said marker is selected from the group consisting of FOXF1, FLK1, BMP4, MOX1 and SDF1.

222. The method of claim 214, wherein said human mesendoderm cells differentiate into definitive endoderm cells in response to said candidate differentiation factor.

223. The method of claim 222, wherein said marker is selected from the group consisting of CXCR4 and SOX17.

224. The method of claim 214, wherein said first time point is prior to providing said candidate differentiation factor to said cell population.

225. The method of claim 214, wherein said first time point is at approximately the same time as providing said candidate differentiation factor to said cell population.

226. The method of claim 214, wherein said first time point is subsequent to providing said candidate differentiation factor to said cell population.

227. The method of claim 214, wherein expression of said marker is increased.

228. The method of claim 214, wherein expression of said marker is decreased.

229. The method of claim 214, wherein expression of said marker is determined by quantitative polymerase chain reaction (Q-PCR).

230. The method of claim 214, wherein expression of said marker is determined by immunocytochemistry.

231. The method of claim 214, wherein said candidate differentiation factor comprises at least one growth factor of the TGFβ superfamily.

232. The method of claim 231, wherein said at least one growth factor of the TGFβ superfamily is activin A.

233. The method of claim 214, wherein said candidate differentiation factor comprises a small molecule.

234. The method of claim 214, wherein said candidate differentiation factor comprises a polypeptide.

235. The method of claim 214, wherein said candidate differentiation factor is not a growth factor of the TGFβ superfamily.

236. The method of claim 214, wherein said candidate differentiation factor is provided to said cell population at a concentration of between about 0.1 ng/ml to about 10 mg/ml.

237. The method of claim 214, wherein said candidate differentiation factor is provided to said cell population at a concentration of between about 1 ng/ml to about 1 mg/ml

238. The method of claim 214, wherein said candidate differentiation factor is provided to said cell population at a concentration of between about 10 ng/ml to about 100 µg/ml.

239. The method of claim 214, wherein said candidate differentiation factor is provided to said cell population at a concentration of between about 100 ng/ml to about 10 µg/ml.

240. The method of claim 214, wherein said candidate differentiation factor is provided to said cell population at a concentration of about 1 µg/ml.

241. A method of increasing the expression of the FGF8 gene product in a human embryonic stem cell (hESC) in vitro, said method comprising obtaining said hESC in a medium comprising less than about 2% (v/v) serum and contacting said hESC with a differentiation factor in an amount sufficient to increase expression of the FGF8 gene product.

242. The method of claim 241, wherein said differentiation factor comprises at least one growth factor of the TGFβ superfamily.

243. The method of claim 242, wherein said differentiation factor comprises activin A.

244. The method of claim 241, wherein said medium lacks serum or lacks serum replacement.

245. A method of increasing the expression of a gene product selected from the group consisting of brachyury, FGF4 and SNAI1 in an human embryonic stem cell (hESC) or a preprimitive streak cell in vitro, said method comprising obtaining said hESC or preprimitive streak cell in a medium comprising less than about 2% (v/v) serum and contacting said hESC or said preprimitive streak cell with a differentiation factor in an amount sufficient to increase expression of a gene product selected from the group consisting of brachyury, FGF4 and SNAI1.

246. The method of claim 245, wherein said differentiation factor comprises at least one growth factor of the TGFβ superfamily.

247. The method of claim 246, wherein said differentiation factor comprises activin A.

248. The method of claim 245, wherein said medium lacks serum or lacks serum replacement.

249. A cell culture comprising human embryonic stem cells (hESCs) and a medium comprising less than about 2% (v/v) serum, wherein said hESCs begin differentiating at a reference time point such that expression of FGF8 mRNA is substantially upregulated as

compared to baseline FGF8 mRNA expression in said hESCs by about 6 hours from said reference time point.

250. The cell culture of claim 249, wherein expression of FGF8 mRNA is downregulated after about 24 hours from said reference time point.

251. The cell culture of claim 250, wherein peak expression of FGF8 mRNA is reached at a time between about 6 hours and about 24 hours from said reference time point.

252. The cell culture of claim 249, wherein β-catenin polypeptide begins to become localized to the cell nucleus by about 17 hours from said reference time point.

253. The cell culture of claim 249, wherein expression of brachyury mRNA is substantially upregulated by about 24 hours from said reference time point.

254. The cell culture of claim 253, wherein expression of brachyury mRNA is substantially downregulated by about 48 hours from said reference time point.

255. The cell culture of claim 254, wherein peak expression of brachyury mRNA is reached at a time between about 12 hours and about 48 hours from said reference time point.

256. The cell culture of claim 255, wherein brachyury mRNA in not substantially expressed by about 72 hours from said reference time point.

257. The cell culture of claim 249, wherein expression of FGF4 mRNA is substantially upregulated by about 24 hours from said reference time point.

258. The cell culture of claim 257, wherein expression of FGF4 mRNA is substantially downregulated by about 48 hours from said reference time point.

259. The cell culture of claim 258, wherein peak expression of FGF4 mRNA is reached at a time between about 12 hours and about 48 hours from said reference time point.

260. The cell culture of claim 259, wherein FGF4 mRNA is not substantially expressed by about 72 hours from said reference time point.

261. The cell culture of claim 249, wherein expression of brachyury and FGF4 mRNA is substantially upregulated by about 24 hours from said reference time point.

262. The cell culture of claim 261, wherein expression of brachyury and FGF4 mRNA is substantially downregulated by about 48 hours from said reference time point.

263. The cell culture of claim 262, wherein peak expression of brachyury and FGF4 mRNA is reached at a time between about 12 hours and about 48 hours from said reference time point.

264. The cell culture of claim 263, wherein brachyury and FGF4 mRNA in not substantially expressed by about 72 hours from said reference time point.

265. The cell culture of claim 249, wherein expression of SNAI1 mRNA is substantially upregulated by about 24 hours from said reference time point.

266. The cell culture of claim 265, wherein expression of SNAI1 mRNA is downregulated by about 48 hours from said reference time point.

267. The cell culture of claim 266, wherein peak expression of SNAI1 mRNA is reached at a time between about 12 hours and about 48 hours from said reference time point.

268. The cell culture of claim 249, wherein expression of E-cadherin mRNA begins to be downregulated by about 12 hours from said reference time point.

269. The cell culture of claim 249, wherein expression of E-cadherin mRNA is substantially downregulated by about 48 hours from said reference time point.

270. The cell culture of claim 249, wherein expression of SOX17 mRNA is substantially upregulated by about 48 hours from said reference time point.

271. The cell culture of claim 249, wherein expression of FOXA2 mRNA is substantially upregulated by about 96 hours from said reference time point.

272. The cell culture of claim 249, wherein said medium comprises less than about 1% (v/v) serum.

273. The cell culture of claim 249, wherein said medium comprises less than about 0.2% (v/v) serum.

274. The cell culture of claim 249, wherein said medium comprises about 0% (v/v) serum.

275. The cell culture of claim 249, wherein said medium lacks serum or lacks serum replacement.

276. The cell culture of claim 249, further comprising a differentiation factor of the TGFβ superfamily.

277. The cell culture of claim 276, wherein said differentiation factor comprises activin A.

278. The cell culture of claim 277, wherein said activin A is present at a concentration of about 100 ng/ml.

279. A cell culture comprising human embryonic stem cells (hESCs), a differentiation factor of the TGFβ superfamily and a medium comprising less than about 2% (v/v) serum.

280. The cell culture of claim 279, wherein in cells of said cell culture, expression of a marker gene selected from the group consisting of FGF8, Nodal, HEG, HEY1, GATA2, BIK and ID1 is upregulated prior to upregulation of expression of a marker gene selected from the group consisting of brachyury, FGF4, SNAI1, Wnt3, MIXL1, DKK4, NETO1, T, DACT1, FLJ22662, SLIT2, GAD1 and GRM4.

281. The cell culture of claim 280, wherein in cells of said cell culture, expression of a marker gene selected from the group consisting of FGF8, Nodal, HEG, HEY1, GATA2, BIK and ID1 is upregulated prior to peak expression of a marker gene selected from the group consisting of brachyury, FGF4, SNAI1, Wnt3, MIXL1, DKK4, NETO1, T, DACT1, FLJ22662, SLIT2, GAD1 and GRM4.

282. The cell culture of claim 281, wherein in cells of said cell culture, expression of a marker gene selected from the group consisting of HEY1, GATA2, BIK and ID1 is downregulated prior to or at about the same time as peak expression of a marker gene selected from the group consisting of brachyury, FGF4, SNAI1, Wnt3, MIXL1, DKK4, NETO1, T, DACT1, FLJ22662, SLIT2, GAD1 and GRM4.

283. The cell culture of claim 279, wherein in cells of said cell culture, expression of a marker gene selected from the group consisting of FGF8, Nodal, HEG, HEY1, GATA2, BIK and ID1 is upregulated prior to upregulation of expression of a marker gene selected from the group consisting of SOX17, FOXA2, CXCR4 and MIXL1.

284. The cell culture of claim 283, wherein in cells of said cell culture, expression of a marker gene selected from the group consisting of brachyury, FGF4, SNAI1, Wnt3, MIXL1, DKK4, NETO1, T, DACT1, FLJ22662, SLIT2, GAD1 and GRM4 is upregulated prior to or at about the same time as upregulation of expression of a marker gene selected from the group consisting of SOX17, FOXA2, CXCR4 and MIXL1.

285. The cell culture of claim 284, wherein in cells of said cell culture, peak expression of a marker gene selected from the group consisting of brachyury, FGF4, SNAI1, Wnt3, MIXL1, DKK4, NETO1, T, DACT1, FLJ22662, SLIT2, GAD1 and GRM4 is reached prior to or at about the same time as upregulation of expression of a marker gene selected from the group consisting of SOX17, FOXA2, CXCR4 and MIXL1.

286. The cell culture of claim 283, wherein in cells of said cell culture, expression of a marker gene selected from the group consisting of FGF8, Nodal, HEG, HEY1, GATA2, BIK and ID1 is upregulated prior to upregulation of expression of a marker gene selected from the group consisting of brachyury, FGF4, SNAI1, Wnt3, MIXL1, DKK4, NETO1, T, DACT1, FLJ22662, SLIT2, GAD1 and GRM4.

287. The cell culture of claim 279, wherein said medium comprises less than about 1% (v/v) serum.

288. The cell culture of claim 279, wherein said medium comprises less than about 0.2% (v/v) serum.

289. The cell culture of claim 279, wherein said medium comprises about 0% (v/v) serum.

290. The cell culture of claim 279, wherein said medium lacks serum or lacks serum replacement.

291. The cell culture of claim 279, wherein said differentiation factor of the TGFβ superfamily comprises activin A.

292. The cell culture of claim 291, wherein said activin A is present in the medium at a concentration of about 100 ng/ml.

293. A method of differentiating cells in a cell culture, said method comprising (a) contacting a cell culture comprising human embryonic stem cells (hESCs) with a medium comprising less that about 2% serum, (b) providing said hESCs with a differentiation factor of the TGFβ superfamily, and (c) permitting differentiation of said hESCs to occur.

294. The method of claim 283, wherein in cells of said cell culture, expression of a marker gene selected from the group consisting of FGF8, Nodal, HEG, HEY1, GATA2, BIK and ID1 is upregulated prior to upregulation of expression of a marker gene selected from the group consisting of brachyury, FGF4, SNAI1, Wnt3, MIXL1, DKK4, NETO1, T, DACT1, FLJ22662, SLIT2, GAD1 and GRM4..

295. The method of claim 294, wherein in cells of said cell culture, expression of a marker gene selected from the group consisting of FGF8, Nodal, HEG, HEY1, GATA2, BIK and ID1 is upregulated prior to peak expression of a marker gene selected from the group consisting of brachyury, FGF4, SNAI1, Wnt3, MIXL1, DKK4, NETO1, T, DACT1, FLJ22662, SLIT2, GAD1 and GRM4.

296. The method of claim 295, wherein in cells of said cell culture, expression of a marker gene selected from the group consisting of HEY1, GATA2, BIK and ID1 is downregulated prior to or at about the same time as peak expression of a marker gene selected from the group consisting of brachyury, FGF4, SNAI1, Wnt3, MIXL1, DKK4, NETO1, T, DACT1, FLJ22662, SLIT2, GAD1 and GRM4.

297. The method of claim 293, wherein in cells of said cell culture, expression of a marker gene selected from the group consisting of FGF8, Nodal, HEG, HEY1, GATA2, BIK and ID1 is upregulated prior to upregulation of expression of a marker gene selected from the group consisting of SOX17, FOXA2, CXCR4 and MIXL1.

298. The method of claim 297, wherein in cells of said cell culture, expression of a marker gene selected from the group consisting of brachyury, FGF4, SNAI1, Wnt3, MIXL1, DKK4, NETO1, T, DACT1, FLJ22662, SLIT2, GAD1 and GRM4 is upregulated prior to or at about the same time as upregulation of expression of a marker gene selected from the group consisting of SOX17, FOXA2, CXCR4 and MIXL1.

299. The method of claim 298, wherein in cells of said cell culture, peak expression of a marker gene selected from the group consisting of brachyury, FGF4, SNAI1, Wnt3, MIXL1, DKK4, NETO1, T, DACT1, FLJ22662, SLIT2, GAD1 and GRM4 is reached prior to or at about the same time as upregulation of expression of a marker gene selected from the group consisting of SOX17, FOXA2, CXCR4 and MIXL1.

300. The method of claim 297, wherein in cells of said cell culture, expression of a marker gene selected from the group consisting of FGF8, Nodal, HEG, HEY1, GATA2, BIK and ID1 is upregulated prior to upregulation of expression of a marker gene selected from the group

consisting of brachyury, FGF4, SNAI1, Wnt3, MIXL1, DKK4, NETO1, T, DACT1, FLJ22662, SLIT2, GAD1 and GRM4.

301. The method of claim 293, wherein said medium comprises less than about 1% (v/v) serum.

302. The method of claim 293, wherein said medium comprises less than about 0.2% (v/v) serum.

303. The method of claim 293, wherein said medium comprises about 0% (v/v) serum.

304. The method of claim 293, wherein said medium lacks serum or lacks serum replacement.

305. The method of claim 293, wherein said differentiation factor of the TGFβ superfamily comprises activin A.

306. The method of claim 305, wherein said activin A is present in the medium at a concentration of about 100 ng/ml.

307. A cell culture comprising human embryonic stem cells (hESCs) and a medium comprising less than about 2% (v/v) serum, wherein said hESCs begin differentiating at a reference time point such that expression of an mRNA selected from the group consisting of FZD10, FGF5 and OCT4 is substantially upregulated as compared to baseline expression of a corresponding mRNA selected from the group consisting of FZD10, FGF5 and OCT4 in said hESCs by about 2 hours from said reference time point.

308. The cell culture of claim 307, wherein said medium comprises less than about 1% (v/v) serum.

309. The cell culture of claim 307, wherein said medium comprises less than about 0.2% (v/v) serum.

310. The cell culture of claim 307, wherein said medium comprises about 0% (v/v) serum.

311. The cell culture of claim 307, wherein said medium lacks serum or lacks serum replacement.

312. The cell culture of claim 307 further comprising a differentiation factor of the TGFβ superfamily.

313. The cell culture of claim 312, wherein said differentiation factor comprises activin A.

314. The cell culture of claim 313, wherein said activin A is present at a concentration of about 100 ng/ml.

315. A cell culture comprising human embryonic stem cells (hESCs) and a medium comprising less than about 2% (v/v) serum, wherein said hESCs begin differentiating at a reference time point such that expression of an mRNA selected from the group consisting of

GBX2, ZFP42 and SOX2 is substantially downregulated as compared to baseline expression of a corresponding mRNA selected from the group consisting of GBX2, ZFP42 and SOX2 in said hESCs by about 2 hours from said reference time point.

316. The cell culture of claim 315, wherein said medium comprises less than about 1% (v/v) serum.

317. The cell culture of claim 315, wherein said medium comprises less than about 0.2% (v/v) serum.

318. The cell culture of claim 315, wherein said medium comprises about 0% (v/v) serum.

319. The cell culture of claim 315, wherein said medium lacks serum or lacks serum replacement.

320. The cell culture of claim 315 further comprising a differentiation factor of the TGFβ superfamily.

321. The cell culture of claim 320, wherein said differentiation factor comprises activin A.

322. The cell culture of claim 321, wherein said activin A is present at a concentration of about 100 ng/ml.

323. A cell culture comprising human embryonic stem cells (hESCs), a differentiation factor of the TGFβ superfamily and a medium comprising less than about 2% (v/v) serum, wherein in cells of said cell culture, expression of a marker gene selected from the group consisting of FZD10, FGF5, Nanog and OCT4 is upregulated or expression of a marker gene selected from the group consisting of GBX2, ZFP42 and SOX2 is downregulated prior to upregulation of expression of a marker gene selected from the group consisting of FGF8, Nodal, HEG, HEY1, GATA2, BIK and ID1.

324. The cell culture of claim 323, wherein expression of a marker gene selected from the group consisting of FZD10, FGF5, Nanog and OCT4 is upregulated or expression of a marker gene selected from the group consisting of GBX2, ZFP42 and SOX2 is downregulated prior to upregulation of expression of a marker gene selected from the group consisting of brachyury, FGF4, SNAI1, Wnt3, MIXL1, DKK4, NETO1, T, DACT1, FLJ22662, SLIT2, GAD1 and GRM4.

325. The cell culture of claim 323, wherein said medium comprises less than about 1% (v/v) serum.

326. The cell culture of claim 323, wherein said medium comprises less than about 0.2% (v/v) serum.

327. The cell culture of claim 323, wherein said medium comprises about 0% (v/v) serum.

328. The cell culture of claim 323, wherein said medium lacks serum or lacks serum replacement.

329. The cell culture of claim 323 further comprising a differentiation factor of the TGFβ superfamily.

330. The cell culture of claim 329, wherein said differentiation factor comprises activin A.

331. The cell culture of claim 330, wherein said activin A is present at a concentration of about 100 ng/ml.

332. A method of differentiating cells in a cell culture, said method comprising (a) contacting a cell culture comprising human embryonic stem cells (hESCs) with a medium comprising less that about 2% serum, (b) providing said hESCs with a differentiation factor of the TGFβ superfamily, and (c) permitting differentiation of said hESCs to occur, wherein in cells of said cell culture, expression of a marker gene selected from the group consisting of FZD10, FGF5, Nanog and OCT4 is upregulated or expression of a marker gene selected from the group consisting of GBX2, ZFP42 and SOX2 is downregulated prior to upregulation of expression of a marker gene selected from the group consisting of FGF8, Nodal, HEG, HEY1, GATA2, BIK and ID1.

333. The method of claim 332, wherein expression of a marker gene selected from the group consisting of FZD10, FGF5, Nanog and OCT4 is upregulated or expression of a marker gene selected from the group consisting of GBX2, ZFP42 and SOX2 is downregulated prior to upregulation of expression of a marker gene selected from the group consisting of brachyury, FGF4, SNAI1, Wnt3, MIXL1, DKK4, NETO1, T, DACT1, FLJ22662, SLIT2, GAD1 and GRM4.

334. The method of claim 332, wherein said medium comprises less than about 1% (v/v) serum.

335. The method of claim 332, wherein said medium comprises less than about 0.2% (v/v) serum.

336. The method of claim 332, wherein said medium comprises about 0% (v/v) serum.

337. The method of claim 332, wherein said medium lacks serum or lacks serum replacement.

338. The method of claim 332 further comprising a differentiation factor of the TGFβ superfamily.

339. The method of claim 338, wherein said differentiation factor comprises activin A.

340. The method of claim 339, wherein said activin A is present at a concentration of about 100 ng/ml.

WHAT IS CLAIMED IS:

1. A method of producing mesendoderm cells, the method comprising the steps of:
obtaining a cell population comprising human pluripotent stem cells;
providing the human pluripotent stem cells with at least one TGFβ superfamily growth factor in an amount sufficient to promote differentiation of the human pluripotent stem cells to mesendoderm cells, said mesendoderm cells being multipotent cells that can differentiate into mesoderm or definitive endoderm
cells; and
allowing sufficient time for the mesendoderm cells to form, wherein the sufficient time for the mesendoderm cells to form has been determined by detecting the presence of mesendoderm cells in the cell population.

2. The method of claim 1, wherein, the TGFβ superfamily growth factor is selected from the group consisting of Nodal, activin A and activin B.

3. The method of claim 2, wherein the TGFβ superfamily growth factor is activin A.

4. The method of claim 3, wherein at least 10 ng/ml activin A is provided.

5. The method of claim 3, wherein at least 100 ng/ml activin A is provided.

6. The method of claim 1, wherein the human pluripotent stem cells comprise human embryonic stem cells.

7. The method of claim 1, wherein the human embryonic stem cells are derived from a tissue selected from the group consisting of the morula, the ICM of an embryo and the gonadal ridges of an embryo.

8. The method of claim 1 further comprising the step of providing serum to the human pluripotent stem cells.

9. The method of claim 1 further comprising a medium that comprises less than about 2% (v/v) serum.

10. The method of claim 1, wherein the expression of the marker selected from the group consisting of brachyury, FGF4 and/or SNAI1 is greater than the expression of the marker selected from the group consisting of OCT4, SOX17, CXCR4, FOXA2, SOX7 and/or SOX1 in the population of mesendoderm cells.

11. The method of claim 1, wherein at least about 15% of the pluripotent human stem cells differentiate into mesendoderm cells.

12. The method of claim 1, wherein at least about 50% of the pluripotent human stem cells differentiate into mesendoderm cells.

13. The method of claim 1, wherein at least about 90% of the pluripotent human stem cells differentiate into mesendoderm cells.

14. The method of claim 1, wherein the said pluripotent human stem cells are further provided with one or more growth factors selected from the group consisting of FGF10, FGF4, FGF2 or Wnt3B.

15. An *in vitro* method of producing human mesendoderm cells, the method comprising:
obtaining a cell population comprising human pluripotent stem cells; and differentiating said cell population in a medium comprising less than about 2% serum and at least one growth factor of the TGFβ superfamily, wherein the growth factor is present in the medium in an amount sufficient to promote differentiation of at least a portion of said pluripotent cells to mesendoderm.

16. The method of claim 15, further comprising allowing sufficient time for the population of mesendoderm cells to form.