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Baca et al.

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(54) **ANTI-VEGF ANTIBODIES**

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- (58) **Field of Classification Search** 424/130.1, 424/133.1, 135.1, 141.1, 155.1, 156.1; 530/387.1, 530/387.3, 388.1, 388.24, 388.8, 388.85

See application file for complete search history.

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Humanized and variant anti-VEGF antibodies and various uses therefor are disclosed. The anti-VEGF antibodies have strong binding affinities for VEGF; inhibit VEGF-induced proliferation of endothelial cells in vitro; and inhibit tumor growth in vivo.

2 Claims, 16 Drawing Sheets

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Variable Heavy

| | | | |
|----------|---|-------|-------|
| A4 .6 .1 | <u>EIQLVQSGPELKQPGETVRISCKASGYTFTNYGMNWVKQAPGKGLKWMG</u> | * | * |
| F(ab)-12 | EVQLVESGGGLVQPGGSLRLSCAASGYTFTNYGMNWVRQAPGKGLEWVG | ***** | ***** |
| humIII | EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVS | | |
| | 1 10 20 30 40 | | |

| | | | |
|----------|---|--------|-------------------|
| A4 .6 .1 | <u>WINTYTGEPTYAADFKRRFTSLETSASTAYLQISNLKNDDTATYFCAK</u> | * * | *** *** *** |
| F(ab)-12 | <u>WINTYTGEPTYAADFKRRFTSLETSKSTAYLQMNSLRAEDTAVYYCAK</u> | ***** | ***** |
| humIII | VISGDGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR | | |
| | 50 a 60 70 80 abc 90 | | |

Fig. 1A

| | | |
|----------|---|-----|
| A4 .6 .1 | <u>YPHYYGSSHWYFDVWGAGTTVTVss</u> (SEQ ID NO: 9) | * |
| F(ab)-12 | <u>YPHYYGSSHWYFDVWGQGTLVTVss</u> (SEQ ID NO: 7) | * |
| humIII | G-----FDYWGQGTLVTVss (SEQ ID NO: 11) | 110 |

Variable Light

| | | |
|----------|---|------|
| A4 .6 .1 | DIQMTQTTSSLASLGDRVIISC <u>SASODISNYLNWYQQKPDGTVKVL</u> IY | **** |
| F(ab)-12 | DIQMTQSPSSLSASVGDRVTIT <u>CASODISNYLNWYQQKPGKAPKV</u> LIY | * |
| humKI | DIQMTQSPSSLSASVGDRVTIT <u>CRASQSISNYLAWYQQKPGKAPKL</u> IY | * |
| | 1 10 20 30 40 | |

Fig. 1B

| | | |
|----------|---|----------------|
| A4 .6 .1 | <u>FTSSLHSGVPSRFSGSGSGTDYSLTISNLEPEDIATYYCQOYSTVPWTF</u> | ** * * * |
| F(ab)-12 | <u>FTSSLHSGVPSRFSGSGSGTDFTLTISSSLQPEDFATYYCQOYSTVPWTF</u> | *** |
| humKI | AASSLES <u>GVPSRFSGSGSGTDFTLTISSSLQPEDFATYYCQQYNSLPWT</u> F | |
| | 50 60 70 80 90 | |

| | | |
|----------|----------------------------|---|
| A4 .6 .1 | GGGTKLEIKR (SEQ ID NO: 10) | * |
| F(ab)-12 | GQGTKVEIKR (SEQ ID NO: 8) | * |
| humKI | GQGTKVEIKR (SEQ ID NO: 12) | |
| | 100 | |

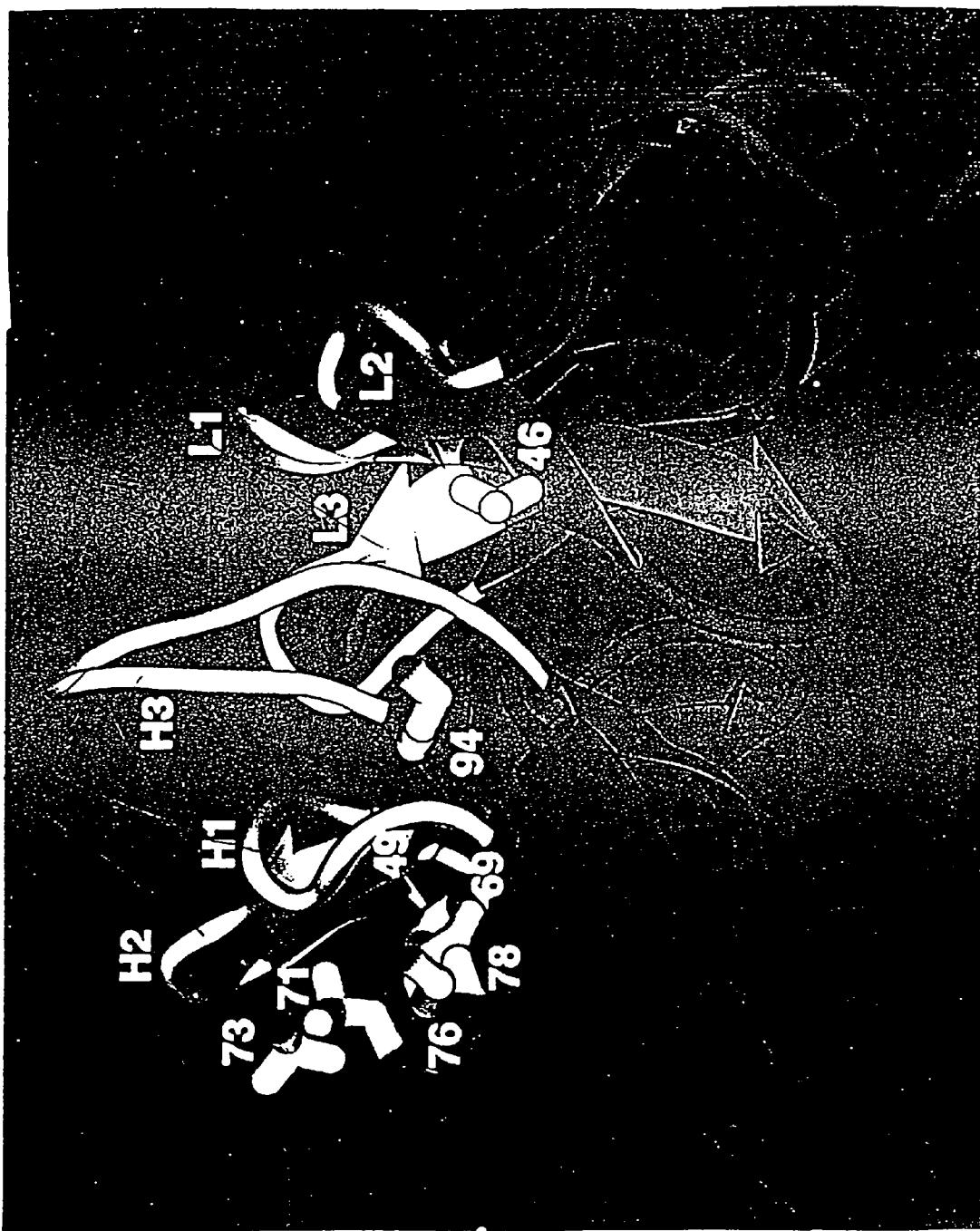


Fig. 2

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