```
Human      MLVDGPSERPALCFLLLAVAMSFFGSALSIDETRAHLLIKEKMMRLGGRLVLNTKEELAN 60
Chimpanzee MLVDGPSERPALCFLLLAVAMSFFGSALSIDETRAHLLLKEKMMRLGGRLVLNTKEELAN 60
           ************************************************************

Human      ERLMTLKIAEMKEAMRTLIFPPSMHFFQAKHLIERSQVFNILRMMPKGAALHLHDIGIVT 120
Chimpanzee ERLMTLKIAEMKEAMRTLIFPPSMHFFQAKHLIERSQVFNILRMMPKGAALHLHDIGIVT 120
           ************************************************************

Human      MDWLVRNVTYRPHCHICFTPRGIMQFRFAHPTPRPSEKCSKWILLEDYRKRVQNVTEFDD 180
Chimpanzee MDWLVRNVTYRPHCHICFTPRGIMQFRFAHPTPRTSEKCSKWILLEDYRKRVQNVTEFDD 180
           ************************************.*********************** 

Human      SLLRNFTLVTQHPEVIYTNQNVVWSKFETIFFTISGLIHYAPVFRDYVFRSMQEFYEDNV 240
Chimpanzee SLLRNFTLVTQHPEVIYTNQNVVWSKFETIFFTISGLIHYAPVFRDYVFRSMQEFYEDNV 240
           ************************************************************

Human      LYMEIRALLLPVYELSGEHHDEEWSVKTYQEVAQKFVETHPEFIGIKIIYSDHRSKDVAV 300
Chimpanzee LYMEIRARLLPVYELSGEHHDEEWSVKTYQEVAQKFVETHPEFIGIKIIYSDHRSKDVAV 300
           ************************************************************

Human      IAESIRMAMGLRIKFPTVVAGFDLVGHEDTGHSLHDYKEALMIPAKDGVKLPYFFHAGET 360
Chimpanzee IAESIRTAMGLRTKFPTVVAGFDLVGHEDTGHSLHDYKEALMIPAKVGVKLPYFFHAGET 360
           ******  ****************************** ************************

Human      DWQGTSIDRNILDALMLNTTRIGHGFALSKHPAVRTYSWKKDIPIEVCPISNQVLKLVSD 420
Chimpanzee DWQGTSIDRNILDALMLNTSRIGHGFALSKHPAVRTYSWKKDIPIEVCPISNQVLKLVSD 420
           ************************:*********************************** 

Human      LRNHPVATLMATGHPMVISSDDPAMFGAKGLSYDFYEVFMGIGGMKADLRTLKQLAMNSI 480
Chimpanzee LRNHPVATLMATGHPMVISSDDPAMFGAKGLSYDFYEVFMGIGGMKADLRTLKQLAMNSI 480
           ************************************************************

Human      KYSTLLESEKNTFMEIWKKRWDKFIADVATK 511
Chimpanzee KYSTLLESEKNTFMEIWKKRWDKFIADVATK 511
           ********************************
```

Figure 1A

```
Human           MLVDGPSERPALCFLLLAVAMSFFGSALSIDETRAHLLLKEKMMRLGGRLVLNTKEELAN 60
Gorilla         MLVDGPSERPALRFLLLAVAMSFFGSALSIDETRAHLLLKEKMMRLGGKLVLNTKEELAN 60
                ************ ************************************************

Human           ERLMTLKIAEMKEAMRTLIFPPSMHFFQAKHLIERSQVFNILRMMPKGAALHLHDIGIVT 120
Gorilla         ERLMTLKIAEMKEAMRTLIFPPSMHFFQAKHLIERSQVFNVLRMMPKGAALHLHDIGIVT 120
                ****************************************:*******************

Human           MDWLVRNVTYRPHCHICFTPRGIMQFRFAHPTPRPSEKCSKWILLEDYRKRVQNVTEFDD 180
Gorilla         MDWLVRNVTYRPHCHICFTPRGIMQFRFAHPTPRTSEKCSKWILLEDYRKQVQNVTEFDD 180
                **********************************.***************:*********

Human           SLLRNFTLVTQHPEVIYTNQNVVWSKFETIFFTISGLIHYAPVFRDYVFRSMQEFYEDNV 240
Gorilla         SLLRNFTLVTQHPEVIYTNQNVVWSKFENIFFTISGLIHYAPVFRDYVFRSMQEFYEDNV 240
                ****************************.*******************************

Human           LYMEIRARLLPVYELSGEHHDEEWSVKTYQEVAQKFVETHPEFIGIKIIYSDHRSKDVAV 300
Gorilla         LYMEIRARLLPVYELSGEHHDEEWSVKTYQEVAQKFVETHPEFIGIKIIYSDHRSKDVAV 300
                ************************************************************

Human           IAESIRMAMGLRIKFPTVVAGFDLVGHEDTGHSLHDYKEALMIPAKDGVKLPYFFHAGET 360
Gorilla         IAESIRTAMGLRTKFPTVVAGFDLVGHEDTGHSLHDYKEALMIPAKDGVKLPYFFHAGET 360
                ****** ***** ********************************************

Human           DWQGTSIDRNILDALMLNTTRIGHGFALSKHPAVRTYSWKKDIPIEVCPISNQVLKLVSD 420
Gorilla         DWQGTSIDRNILDALMLNTTRIGHGFALSKHPAVRTYSWKKDIPIEVCPISNQVLKLVSD 420
                ************************************************************

Human           LRNHPVATLMATGHPMVISSDDPAMFGAKGLSYDFYEVFMGIGGMKADLRTLKQLAMNSI 480
Gorilla         LRNHPVATLMATGHPMVISSDDPAMFGAKGLSYDFYEVFMGIGGMKADLRTLKQLAMNSI 480
                ************************************************************

Human           KYSTLLESEKNTFMEIWKKRWDKFIADVATK 511
Gorilla         KYSTLLESEKNTFMEIWKKRWDKFIADVATK 511
                ********************************
```

Figure 1B

```
Human       MLVDGPSERPALCFLLLAVAMSFFGSALSIDETRAHLLLKEKMMRLGGRLVLNTKEELAN 60
Pygmy_chimp MLVDGPSERPALCFLLLAVAMSFFSSALSIDETRAHLLLKEKMMRLGGRLVLNTKEELAN 60
            ************************.*************************************

Human       ERLMTLKIAEMKEAMRTLIFPPSMHFFQAKHLIERSQVFNILRMMPKGAALHLHDIGIVT 120
Pygmy_chimp ERLMTLKIAEMKEAMRTLIFPPSMHFFQAKHLIERSQVFNILRMMPKGAALHLHDIGIVT 120
            ************************************************************

Human       MDWLVRNVTYRPHCHICFTPRGIMQFRFAHPTPRPSEKCSKWILLEDYRKRVQNVTEFDD 180
Pygmy_chimp MDWLVRNVTYRPHCHICFTPRGIMQFRFAHPTPRTSEKCSKWILLEDYRKRVQNVTEFDD 180
            ************************************.*********************** 

Human       SLLRNFTLVTQHPEVIYTNQNVVWSKFETIFFTISGLIHYAPVFRDYVFRSMQEFYEDNV 240
Pygmy_chimp SLLRNFTLVTQHPEVIYTNQNVVWSKFETIFFTISGLIHYAPVFRDYVFRSMQEFYEDNV 240
            ************************************************************

Human       LYMEIRARLLPVYELSGEHHDEEWSVKTYQEVAQKFVETHPEFIGIKIIYSDHRSKDVAV 300
Pygmy_chimp LYMEIRARLLPVYELSGEHHDEEWSVKTYQEVAQKFVETHPEFIGIKIIYSDHRSKDVAV 300
            ************************************************************

Human       IAESIRMAMGLRIKFPTVVAGFDLVGHEDTGHSLHDYKEALMIPAKDGVKLPYFFHAGET 360
Pygmy_chimp IAESIRTAMGLRTKFPTVVAGFDLVGHEDTGHSLHDYKEALMIPAKVGVKLPYFFHAGET 360
            ****** ****** ************************** ************** ******

Human       DWQGTSIDRNILDALMLNTTRIGHGFALSKHPAVRRTYSWKKDIPIEVCPISNQVLKLVSD 420
Pygmy_chimp DWQGTSIDRNILDALMLNASRIGHGFALSKHPAVRRTYSWEKDIPIEVCPISNQVLKLVSD 420
            **********::**********************:********************** 

Human       LRNHPVATLMATGHPMVISSDDPAMFGAKGLSYDFYEVFMGIGGMKADLRTLKQLAMNSI 480
Pygmy_chimp LRNHPVATLMATGHPMVISSDDPAMFGAKGLSYDFYEVFMGIGGMKADLRTLKQLAMNSI 480
            ************************************************************

Human       KYSTLLESEKNTFMEIWKKRWDKFIADVATK 511
Pygmy_chimp KYSTLLESEKNTFMEIWKKRWDKFIADVATK 511
            ********************************
```

Figure 1C

```
Human       MLVDGPSERPALCFLLLAVAMSFFGSALSIDETRAHLLIKEKMMRLGGRLVLNTKEELAN 60
Orangutan   MLVDGPSEWPALRFLLLAVAMSFFGSALSIDETRAHLLLKEKMMRLGGRLVLNTKEEQAN 60
            ********* *** ********************************************* **

Human       ERLMTLKIAEMKEAMRTLIFPPSMHFFQAKHLIERSQVFNILRMMPKGAALHLHDIGIVT 120
Orangutan   ERLMMLKIAEMKEAMRTLIFPPSMHFFQAKHLIERSQVFNILRMMPKGAALHLHDIGIVT 120
            *****  ************************************************** ****

Human       MDWLVRNVTYRPHCHICFTPRGIMQFRFAHPTPRPSEKCSKWILLEDYRKRVQNVTEFDD 180
Orangutan   MDWLVRNVTYRPHCHICFTPKGIMQFRFAHPTPRTSEKCSKWILLEDYRKRVQNVTEFDD 180
            ********************:*********************.********************

Human       SLLRNFTLVTQHPEVIYTNQNVVWSKFETIFFTISGLIHYAPVFRDYVFRSMQEFYEDNV 240
Orangutan   SLLRNFTLVTQHPEVIYTNQNVVWSKFETIFFTISGLIHYAPVFRDYVFQSMQEFYEDNV 240
            ************************************************:***********

Human       LYMEIRALLLPVYELSGEHHDEEWSVKTYQEVAQKFVETHPEFIGIKIIYSDHRSKDVAV 300
Orangutan   LYMEIRARLLPVYELSGEHHDEEWSVKTYQEVAQKFVETHPEFIGIKIIYSDHRSKDVAV 300
            ************************************************************

Human       IAESIRMAMGLRIKFPTVVAGFDLVGHEDTGHSLHDYKEALMIPAKDGVKLPYFFHAGET 360
Orangutan   IAESIRTAMGLRTKFPTVVAGFDLVGREDTGHSLQDYKEALMIPAKGGVKLPYFFHAGET 360
            ******  ****************:*********:**************.************

Human       DWQGTSIDRNILDALMLNTTRIGHGFALSKHPAVRTYSWKKDIPIEVCPISNQVLKLVSD 420
Orangutan   DWQGTSIDRNILDALMLNTTRIGHGFALSKHPAVRAYSWKKDIPIEVCPISNQVLKLVSD 420
            ************************************:*********************** 

Human       LRNHPVATLMATGHPMVISSDDPAMFGAKGLSYDFYEVFMGIGGMKADLRTLKQLAMNSI 480
Orangutan   LRNHPVATLMATGHPMVISSDDPAIFGAKGLSYDFYEVFMGIGGMKADLRTLKQLAMNSI 480
            **********************:*************************************

Human       KYSTLLESEKNTFMEIWKKRWDKFIADVATK 511
Orangutan   KYSALLEIEKNTFMEIWKKRWDKFIADVATK 511
            ***:*** ********************
```

Figure 1D


Human MLVDGPSERPALCFLLLAVAMSFFGSALSIDETRAHLLLKEKMMRLGGRLVLNTKEELAN 60
Gibbon MLVDGPSEWPALRFLLLAVAMSFFGSALSIDETRAHLLLKEKMMRLGGKLVLSTKEEQAN 60
Human ERLMTLKIAEMKEAMRTLIFPPSMHFFQAKHLIERSQVFNILRMMPKGAALHLHDIGIVT 120
Gibbon ERLMTLKITEMKEAMKTLIFPPSMHFFQAKHLIERSQVFNILRMMPKGAALHLHDIGIVT 120
Human MDWLVRNVTYRPHCHICFTPRGIMQFRFAHPTPRPSEKCSKWILLEDYRKRVQNVTEFDD 180
Gibbon MDWLVRNVTYRPHCHICFTPKGIMQFRFAHPTPRTSEKCSKWILLEDYRKRVQNVTEFDD 180
Human SLLRNFTLVTQHPEVIYTNQNVVWSKFETIFFTISGLIHYAPVFRDYVFRSMQEFYEDNV 240
Gibbon SLLRNFTLVTQHPEVIYTNQNVVWSKFETIFFTISGLIHYAPVFRDYVFX-------DNV 233
Human LYMEIRARLLPVYELSGEHHDEEWSVKTYQEVAQKFVETHPEFIGIKIIYSDHRSKDVAV 300
Gibbon LYMEIRARLLPVYELSGEHHDEEWSVKTYQEVAQKFVETHPEFIGIKIIYSDHRSKDVAV 293
Human IAESIRMAMGLRIKFPTVVAGFDLVGHEDTGHSLHDYKEALMIPAKDGVKLPYFFHAGET 360
Gibbon IAESIRTAMGLRAKFPTVVAGFDLVGHEDTGHSLHDYKEALMIPTKDGVKLPYFFHAGET 353
Human DWQGTSIDRNILDALMLNTTRIGHGFALSKHPAVRTYSWKKDIPIEVCPISNQVLKLVSD 420
Gibbon DWQGTSIDKNILDALMLNTTRIGHGFALSKHPAVRAYSWKKDIPIEVCPISNQVLKLVSD 413
Human LRNHPVATLMATGHPMVISSDDPAMFGAKGLSYDFYEVFMGIGGMKADLRTLKQLAMNSI 480
Gibbon LRNHPVATLMATGHPMVISSDDPAIFGAKGLSYDFYEVFMGIGGMKADLRTLKQLAMNSI 473
Human KYSTLLESEKNTFMEIWKKRWDKFIADVATK 511
Gibbon KYSTLLETEKNTFMEIWKKRWDKFIADVATK 504

Figure 1E

```
Human     MLVDGPSERPALCFLLLAVAMSFFGSALSIDETRAHLLLKEKMMRLGGRLVLNTKEELAN 60
Macaque   MLVDGPSEWPALRFLLLAVAMSFFRSALSIDE--AHLLLKEKMMRLGGRLVLTTKEEQAN 58
          ********* *** ********************  ********************* ***.**** **

Human     ERLMTLKIAEMKEAMRTLIFPPSMHFFQAKHLIERSQVFNILRMMPKGAALHLHDIGIVT 120
Macaque   ERLMTLKIAEMKEAMKTLIFPPSMHFFQAKHLIERSQVFNILRMMPKGAALHLHDTGIVT 118
          ************************:*********************************** ****

Human     MDWLVRNVTYRPHCHICFTPRGIMQFRFAHPTPRPSEKCSKWILLEDYRKRVQNVTEFDD 180
Macaque   MDWLVRNVTYRPHCHICFTSKGIMQFRFAHPTPRTSEKCSKWILLEDYRKRVQNVTEFDD 178
          ************************.*********************************

Human     SLLRNFTLVTQHPEVIYTNQNVVWSKFETIFFTISGLIHYAPVFRDYVFRSMQEFYEDNV 240
Macaque   SLLRNFTLVTQHPEVIYTNQNVVWSKFQTIFFTISGLIRYAPVFRDYVFRSMQEFYEDNV 238
          ************************:**********:*********************

Human     LYMEIRARLLPVYELSGEHHDEEWSVKTYQEVAQKFVETHPEFIGIKIIYSDHRSKDVAV 300
Macaque   LYMEIRARLLPVYELSGEHHDEEWSVKTYQEVAQKFVETHPEFIGIKIIYSDDRSKDVTV 298
          ************************************************.******:*

Human     IAESIRMAMGLRIKFPTVVAGFDLVGHEDTGHSLHDYKEALMIPAKDGVKLPYFFHAGET 360
Macaque   IAESIRTAMGLRTKFPTVVAGFDLVGHEDTGHSLHYYKEALMIPARDGGKLPYFFHAGET 358
          ****** ***** ************************ **********:** **********

Human     DWQGTSIDRNILDALMLNTTRIGHGFALSKHPAVRTYSWTKDIPIEVCPISNQVLKLVSD 420
Macaque   DWQGTSIDKNILDALMLNTTRIGHGFALSKHPAARAYSWEKDIPIEVCPISNQVLKLVSD 418
          *********:************************.*:****:********************

Human     LRNHPVATLMATGHPMVISSDDPAMFGAKGLSYDFYEVFMGIGGMKADLRTLKQLAMNSI 480
Macaque   LRNHPVAALMAIGHPMVISSDDPAMFGAKGLSYDFYEAFMGIGGMKADLRTLKQLAMNSI 478
          ********:*** ************************.********************

Human     KYSTLLESEKNTFMEIWKKRWDKFIADVATK 511
Macaque   KYSTLLETEKNTFMEIWKKRWDKFIADVATK 509
          :*******:*********************
```

Figure 1F

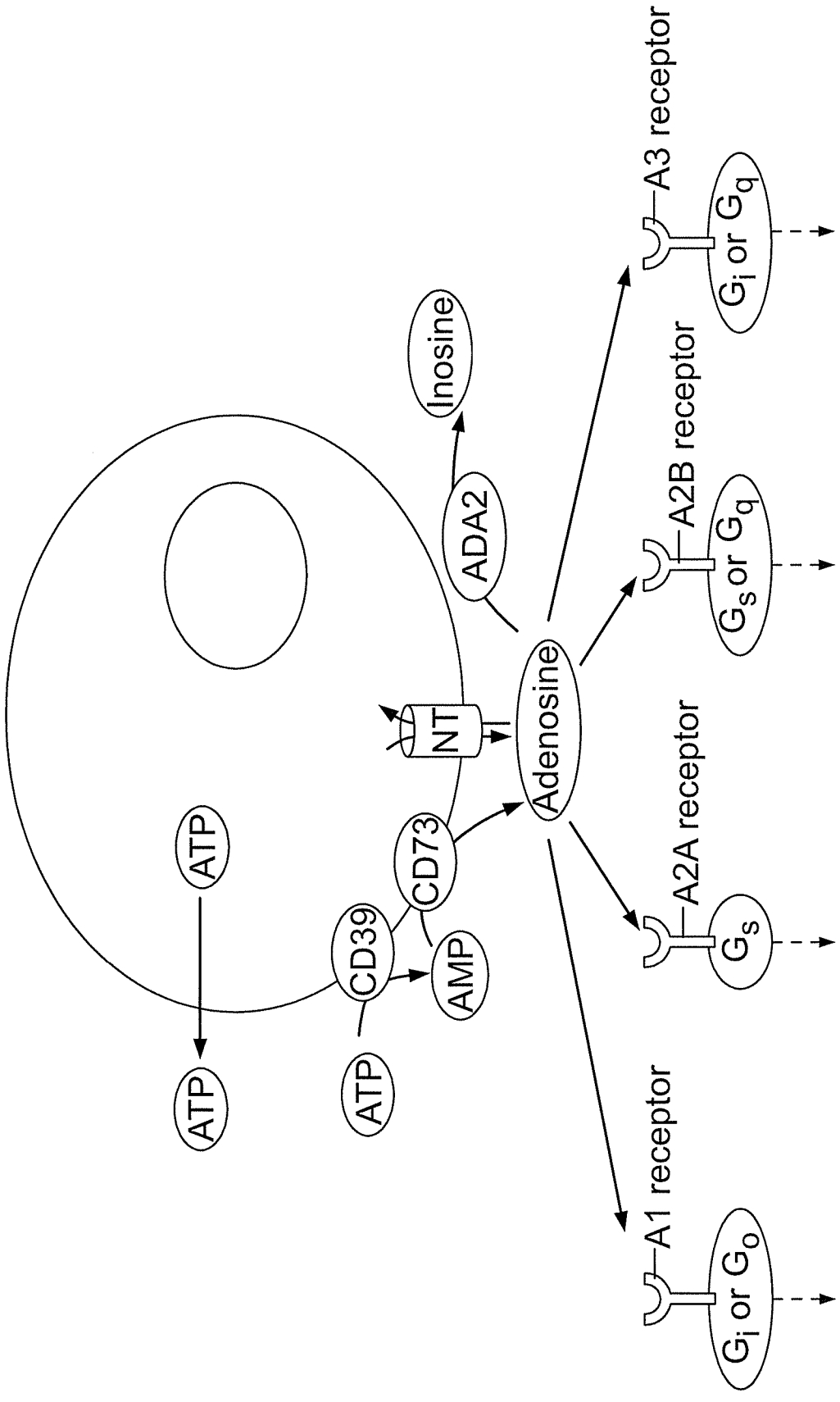

ATP
ATP
ATP
CD39
CD73
AMP
NT
Adenosine
ADA2
Inosine
A1 receptor
A2A receptor
A2B receptor
A3 receptor
G_i or G_o
G_s
G_s or G_q
G_i or G_q
adenosine-mediated activities such as immunosuppression, cancer cell proliferation, cancer cell migration and/or metastasis, angiogenesis and other effects

Figure 2