

| INFORME DE BÚSQUEDA DE PATENTES                                                                                                                                                                                                                                                                                                                                               |                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                       |                                                    |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|----------------------------------------------------|
| N° de solicitud: NC2017/0002166                                                                                                                                                                                                                                                                                                                                               |                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                       |                                                    |
| CRITERIOS PARA LA BÚSQUEDA (Anexar pantallazo o reporte en PDF, junto con los boléanos utilizados*. Para el caso de secuencias, anexar alineamientos)                                                                                                                                                                                                                         |                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                       |                                                    |
| Palabras clave utilizadas                                                                                                                                                                                                                                                                                                                                                     |                                 | IL-2, IL-2RA, interleukin 2, interleukin 2 receptor, fusion protein, half-life extension, (Gly3Ser)3 linker                                                                                                                                                                                                                                                                                                                                                                   |                                                       |                                                    |
| CLASIFICACIONES UTILIZADAS PARA LA BÚSQUEDA                                                                                                                                                                                                                                                                                                                                   |                                 | CIP: A61K 38/00, C07K 14/55                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                       |                                                    |
| DOCUMENTOS CONSIDERADOS RELEVANTES (documentos patentes, literatura no patente, etc...)                                                                                                                                                                                                                                                                                       |                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                       |                                                    |
| Informes/Base de datos                                                                                                                                                                                                                                                                                                                                                        | N° de solicitud/ Autor          | Fecha de Publicación/Presentación (DD/MM/AAAA)                                                                                                                                                                                                                                                                                                                                                                                                                                | Reiv. afectadas                                       | Categorías especiales de los documentos citados*** |
| SIPI                                                                                                                                                                                                                                                                                                                                                                          | 14241630                        | 13/02/2014                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | -                                                     | A                                                  |
|                                                                                                                                                                                                                                                                                                                                                                               | 15242704                        | 25/09/2014                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | -                                                     | A                                                  |
|                                                                                                                                                                                                                                                                                                                                                                               | 16131989                        | 13/08/2015                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | -                                                     | A                                                  |
| ISA (EPO)                                                                                                                                                                                                                                                                                                                                                                     | Puskas <i>et al.</i> (2011)     | 23/06/2011                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | -                                                     | A                                                  |
|                                                                                                                                                                                                                                                                                                                                                                               | WO 2011/123683                  | 06/10/2011                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 8 y 12<br>(Pág. 36, reiv. 15 y 16, pág. 38, reiv. 28) | X                                                  |
|                                                                                                                                                                                                                                                                                                                                                                               | WO 2014/023752                  | 13/02/2014                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | -                                                     | A                                                  |
|                                                                                                                                                                                                                                                                                                                                                                               | Millington <i>et al.</i> (2012) | 01/04/2012                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | -                                                     | A                                                  |
|                                                                                                                                                                                                                                                                                                                                                                               | Melder <i>et al.</i> (2005)     | 01/06/2005                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | -                                                     | A                                                  |
|                                                                                                                                                                                                                                                                                                                                                                               | Stoklasek <i>et al.</i> (2006)  | 01/11/2006                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | -                                                     | A                                                  |
|                                                                                                                                                                                                                                                                                                                                                                               | Wilkinson <i>et al.</i> (2007)  | 01/09/2007                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | -                                                     | A                                                  |
|                                                                                                                                                                                                                                                                                                                                                                               | Malek <i>et al.</i> (2010)      | 01/08/2010                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | -                                                     | A                                                  |
| USPTO                                                                                                                                                                                                                                                                                                                                                                         | US 2006/0263857                 | 23/11/2006                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | -                                                     | A                                                  |
| *** Categorías especiales de documentos citados:                                                                                                                                                                                                                                                                                                                              |                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                       |                                                    |
| “A” documento que define el estado general de la técnica no considerado como particularmente relevante.<br>“E” solicitud de patente o patente anterior pero publicada en la fecha de presentación internacional o en fecha posterior.<br>“P” documento publicado antes de la fecha de presentación internacional pero con posterioridad a la fecha de prioridad reivindicada. |                                 | “X” documento particularmente relevante; la invención reivindicada no puede considerarse nueva o que implique una actividad inventiva por referencia al documento aisladamente considerado.<br>“Y” documento particularmente relevante; la invención reivindicada no puede considerarse que implique una actividad inventiva cuando el documento se asocia a otro u otros documentos de la misma naturaleza, cuya combinación resulta evidente para un experto en la materia. |                                                       |                                                    |
| **** Indicar entre paréntesis la Autoridad que realizó la búsqueda o el informe preliminar Ejs: EPO, JP, INAPI.                                                                                                                                                                                                                                                               |                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                       |                                                    |

|                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|-----------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Literatura no patente | <p>Puskas, J., Skrombolas, D., Sedlacek, A., Lord, E., Sullivan, M., Frelinger, J. 2011. Development of an attenuated interleukin-2 fusion protein that can be activated by tumour-expressed proteases. <i>Immunology</i>, Vol. 133 (2), Pág: 206-220.</p> <p>Millington, T., Koulmanda, M., Ng, C., Boskovic, S., Nadazdin, O. M., Benichou, G., Xiao Zheng, X., Strom, T. B., Madsen, J. C. 2012. Effects of an agonist interleukin-2/Fc fusion protein, a mutant antagonist interleukin-15/Fc fusion protein, and sirolimus on cardiac allograft survival in non-human primates. <i>J Heart Lung Transplant.</i>, Vol. 31 (4), Pág: 427-435.</p> <p>Melder, R. J., Osborn, B. L., Riccobene, T., Kanakaraj, P., Wei, P.,</p> |
|-----------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

Chen, G., Stolow, D., Green Halpern, W., Migone, T., Wang, Q., Grzegorzewski, K. J., Gallant, G. 2005. Pharmacokinetics and in vitro and in vivo anti-tumor response of an interleukin-2-human serum albumin fusion protein in mice. *Cancer Immunol Immunother*, Vol. 54 (6), Pág: 535-547.

Stoklasek, T. A., Schluns, K. S., Lefrançois, L. 2006. Combined IL-15/IL-15R $\alpha$  Immunotherapy Maximizes IL-15 Activity In Vivo. *J Immunol*, Vol. 177 (9), Pág: 6072-6080.

Wilkinson, I. R., Ferrandis, E., Artymiuk, P. J., Teillot, M., Soulard, C., Touvay, C., Pradhananga, S. L., Justice, S., Wu, Z., Leung, K. C., Strasburger, C. J., Sayers, J. R., Ross, R. J. 2007. A ligand-receptor fusion of growth hormone forms a dimer and is a potent long-acting agonist. *Nat Med.*, Vol. 13 (9), Pág: 1108-1113.

Malek, T. R., Castro, I. 2010. Interleukin-2 Receptor Signaling: At the Interface between Tolerance and Immunity. *Immunity*, Vol. 33 (2), Pág: 153-165.

Fecha del reporte de búsqueda:

24/octubre/2018

## Búsqueda en PatBase



Username: SIC11@patbase.com  
Subaccount: Tatiana Vargas

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| #  | Search query                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Results | Options                                   |
|----|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|-------------------------------------------|
| 16 | SFT=((interleukin) and (interleukin w2 receptor) and ((fusion w2 protein*) or (chimer* w2 protein*)))                                                                                                                                                                                                                                                                                                                                                                                                                              | 2       | View   Browse   Hits   Optimise   more... |
| 15 | SFT=(2 and ("GGGSGGGSGGG" or (Gly3Ser) or (GGGS) or (G3S))) and PD<20140806                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 194     | View   Browse   Hits   Optimise   more... |
| 14 | SFT=(2 and GGGSGGGSGGG) and PD<20140806                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 3       | View   Browse   Hits   Optimise   more... |
| 13 | SFT=((IL-2 and IL-2r w3 (fusion or chimer*)) and PD<20140806                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 4       | View   Browse   Hits   Optimise   more... |
| 12 | SFT=(11 and (fusion w3 protein*)) and PD<20140806                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 685     | View   Browse   Hits   Optimise   more... |
| 11 | SFT=((IL-2/IL-2r) or (IL2/IL2r) or (IL2 w5 IL2r)) and PD<20140806                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 1008    | View   Browse   Hits   Optimise   more... |
| 10 | STAC=(8 and (IL-2 or IL2 or "Interleukin 2" or (Interleukin?2)) and (cd25 or IL-2R or IL-2RA)) and PD<20140806                                                                                                                                                                                                                                                                                                                                                                                                                     | 16      | View   Browse   Hits   Optimise   more... |
| 9  | SFT=(8 and (IL-2 or IL2 or "Interleukin 2" or (Interleukin?2)) and (cd25 or IL-2R or IL-2RA)) and PD<20140806                                                                                                                                                                                                                                                                                                                                                                                                                      | 179     | View   Browse   Hits   Optimise   more... |
| 8  | SFT=(5 and (increas* or exten* or prolong*) and (Half?life or (half w3 life) or (half w3 liv*)) ) and PD<20140806                                                                                                                                                                                                                                                                                                                                                                                                                  | 179     | View   Browse   Hits   Optimise   more... |
| 7  | [SP]: 1. a fusion protein comprising: (a) a first polypeptide comprising interleukin-2 (IL-2) or a functional variant or fragment thereof and(b) a second polypeptide, fused in frame to said first polypeptide, said second polypeptide comprises an extracellular domain of interleukin-2 receptor alpha (IL-2ra) or a functional variant or fragment thereof, wherein said fusion protein has IL-2 activity. 2. the fusion protein of claim 1, wherein said fusion protein has an increased IL-2 potency wh... show full search | 0       |                                           |
| 6  | SFT=(5 and (increas* or exten* or prolong*) and (Half?life or (half w3 life) or (half w3 liv*)) )                                                                                                                                                                                                                                                                                                                                                                                                                                  | 323     | View   Browse   Hits   Optimise   more... |
| 5  | SFT=(4 and (GGGS or G3S or Gly3Ser) or (GGGS)))                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 424     | View   Browse   Hits   Optimise   more... |
| 4  | SFT=(3 and (linker))                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 4118    | View   Browse   Hits   Optimise   more... |
| 3  | SFT=(2 and ((fusion w3 protein*) or (chimer* w3 protein*)))                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 5830    | View   Browse   Hits   Optimise   more... |
| 2  | SFT=((IL-2 or IL2 or "Interleukin 2" or (Interleukin?2)) and (cd25 or IL-2R or IL-2RA))                                                                                                                                                                                                                                                                                                                                                                                                                                            | 9615    | View   Browse   Hits   Optimise   more... |
| 1  | SFT=((IL-2 or IL2 or "Interleukin 2" or (Interleukin?2)))                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 73943   | View   Browse   Hits   Optimise   more... |

## Búsqueda en Epoquenet

[EPODOC: SS 1] (IL 2W "2") OR (INTERLEUKIN?2)

Results in EPODOC 3.328

[SS 2] 1 AND (IL?2R)

Results in EPODOC 1

[SS 3] ..LI



1/1 © EPODOC / EPO

PN - [WO2017184901](#) A1 20171026

PR - US201662325428P 20160420

AP - WO2017US28693 20170420

DT - \*; Rep

CT - |EP| ISR (A1)

[XP055382781](#) A[XY];

[WO9422914](#) A1 19941013 [XY] (HUTCHINSON FRED CANCER RES [US], et al)

[X] 1,2,4-6,9,10,12-15,17-19,21,39-46,48,58-64,66

\* page 1, line 24 - line 29; figures 2,5; examples 8,9; claims 1-43 \*

\* page 4, line 5 - line 15 \*

\* page 7, line 12 - line 28 \*

\* page 11, line 9 - page 12, line 15 \*

\* the whole document \*

[Y] 3,7,8,11,16,20,22-38,47,51-56;

[XP055382318](#) A[Y];

[XP002771214](#) A[Y];

[XP002771215](#) A[Y];

[XP055383506](#) A[Y]

CTNP - |EP| ISR (A1)

[XY] - LAWRENCE S. EVANS ET AL, "Expression of Chimeric Granulocyte-Macrophage