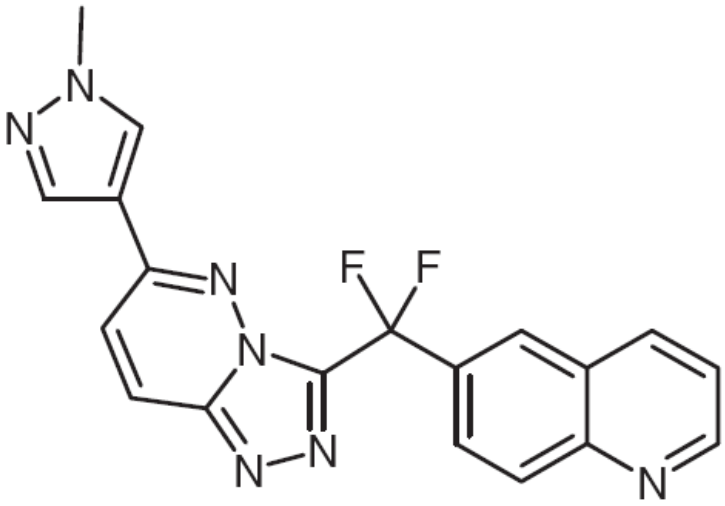
EXON	LEFT PRIMER	RIGHT PRIMER	SEQUENCING PRIMER
Exon 1-1	ATCCTCTAGGGTCCCAGCTC	CAGGCTCTGGACAGACTTCA	ACTTCAGGTCAGGCCCAAG
Exon 1-2	CTACGAGGGCGACAGAAATG	TATGGTGGGCTGAGAAGAGG	GAGGGCGACAGAAATGAGAG
Exon 1-3	TGCTTCCTGCATGACCTAGA	CTTGGGCAGCACTGACAAC	GCACTGACAACGCCACAA
Exon 1-4	AGCCCACGCTCAGTGTCTAT	GCTCAGCTCAGTGGCAAGTT	AGCACAGGGTAGGGCTGTC
Exon 1-5	TGGTCCTCGACTGCAGATTT	ACTGGGCGACTGGAAGAAGT	TCAATTAGTGTGTCCAGCAGGT
Exon 1-6	GGTCTTTGTGACTGGCAAGG	CCTCAGTGATGGAAGGGAAG	CCCCAACTCTGTCGTCTGTG
Exon 2	CACAAGGCTGAACCCTGACT	CTAGGGGACTGTGGGGATG	CTTCCCTTCCCTGACCTTTC
Exon 3	GTCCTCATCCCCACAGTCC	ATGTCAATGCCTCCCTGGAT	TCTCCATCCCCATTTTGCT
Exon 4	GCCCTACCACCCTAGCCTAC	CTGCCAGGGAAGCCATAC	CCCTAGCCTACTGTGTACCG
Exon 5	AGGTGGGGCTGAGAGAGC	AGGGGAGGGACCAGATTGTA	CACATGAGGACTCAGGCTGT
Exon 6	GAGGCATGGGTGGAGAAAT	GCTTAGGCAGGTCCTCCAC	AAATGCCATTCTCTGGCTCA
Exon 7	GCTACCTTGCCCTGTCTGTG	GGGCTGAAGAGGGCAGTAGT	GGTCCCCACCTGGATAGAAC
Exon 8	TGGCCATCACAAAGAGGGTA	CTTTGGGTGTTCTCCAAAGC	TGAGCCCAATCTCTTGTTCC
Exon 9	ATGAGAGAGCCAGCTTTGGA	CTGCAGCTCAGGGAACTCAT	GAGCCAGCTTTGGAGAACAC
Exon 10	GGAGGAAGGCTGGATGAGTT	GTAGGCTGGCCCCTACTTTC	GGGGTTCCTGGCTAATCACT
Exon 11	ACCCAGTGCCAACCTAGTTC	CCCAGGATATGACATTCACCA	CACTGAAGCCTGAGGAGCAT
Exon 12	GGACCTCCCTGGGAAACAC	GGGTAGGGGCTGATTAAAGG	CTACAGGCTGGGCCTGAGTT
Exon 13	GGATCTAAGTCCTCCCCAGAG	GGAGAGGGAATGAGGAGCTT	CAAGCCACCAAGGATTCTCT
Exon 14	CCACACCCCTGCCTATTCT	TTTCACTGTGTTAGCCAGGAC	GATAGTGGAGGCATGAGAAGC
Exon 15	TCTGAGGTCTGGTTGCCAAT	CTCTGCCTTCCCATCTTCTG	GCCAATGAGAATGTGTGGTG
Exon 16	CCTGAGCAGGAGACCTTCAT	ACCCAGAGCCAGATGAACAC	CTGCCCTGTGCCTGACTT
Exon 17	CAGTGTTCATCTGGCTCTGG	AGCACCGCACACCCTCAT	TGCTTCACCCCAGCTACTCT
Exon 18	TGGGTTCAGGGCCTGGTA	AAGCCATGTGGACTGTAGGG	AGGGCCAGTCCTAAGTGTGA
Exon 19	ATTTGGGGTGAGTTGAGTCC	GCTCTGTCTCCTGTCTCTTCCA	AGTTCCCTCCCCACTACCAC
Exon 20-1	CAGAATCCTTGGGTGGAAAT	TGGACGCACATTCATCTCAT	CTTGGGTGGAAATTGCCTTA
Exon 20-2	GGGAGGTGGAGCAGATAGTG	CTCAAGGCAGCTAAGCAGGT	CACTGCTTGGGGACCATTAT

Supplementary table 1. Primers used to amplify (Left and Right) and sequence (Sequencing) *Ron* entire coding sequence (exons 1 to 20). Exons larger than 300 bp (i.e. exons 1 and 20) were subdivided into smaller amplify products.



Supplementary figure 1.

Chemical structure of the JNJ-38877605 *Met* inhibitor.

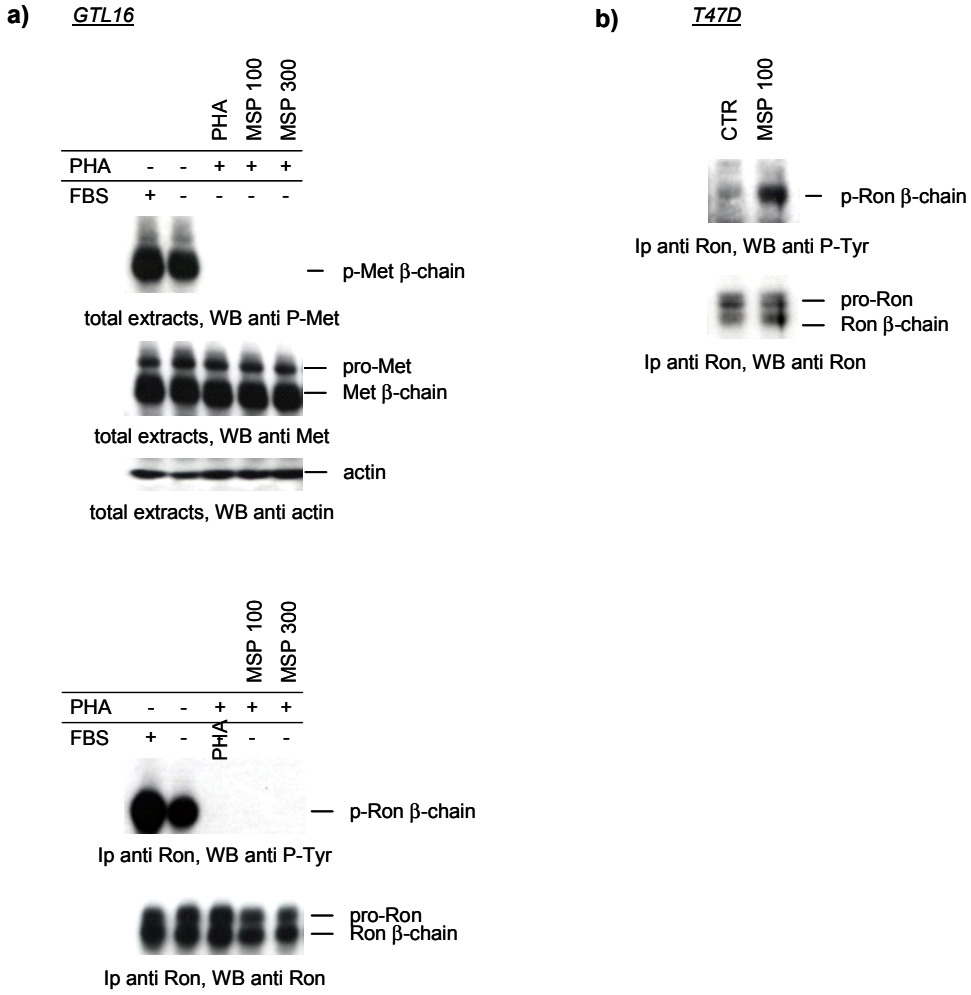
- Chemical Formula: $C_{19}H_{13}F_2N_7$.
- Molecular Weight: 377.35 Dalton.
- Registry Number: 943540-75-8.
- Synthesis & NMR data described in the patent WO2007075567.
- Highly specific MET inhibitor (selective over more than 250 kinases tested).
- ATP competitor.
- Enzyme IC_{50}: 4 nM.
- Phospho-MET IC_{50}: 50 nM.

References

1. Perera,T., Lavrijssen,T., and Janssens,B. 2008. JNJ-38877605: a selective Met kinase inhibitor inducing regression of Met driven tumor models. *99th AACR Annual Meeting; 2008 Apr 12-16; San Diego (CA)*. 4837 (Abstr.)

2. Comoglio, P.M., Giordano, S., and Trusolino, L. 2008. Drug development of MET inhibitors: targeting oncogene addiction and expedience. *Nat. Rev. Drug Discov.* **7**:504-516.

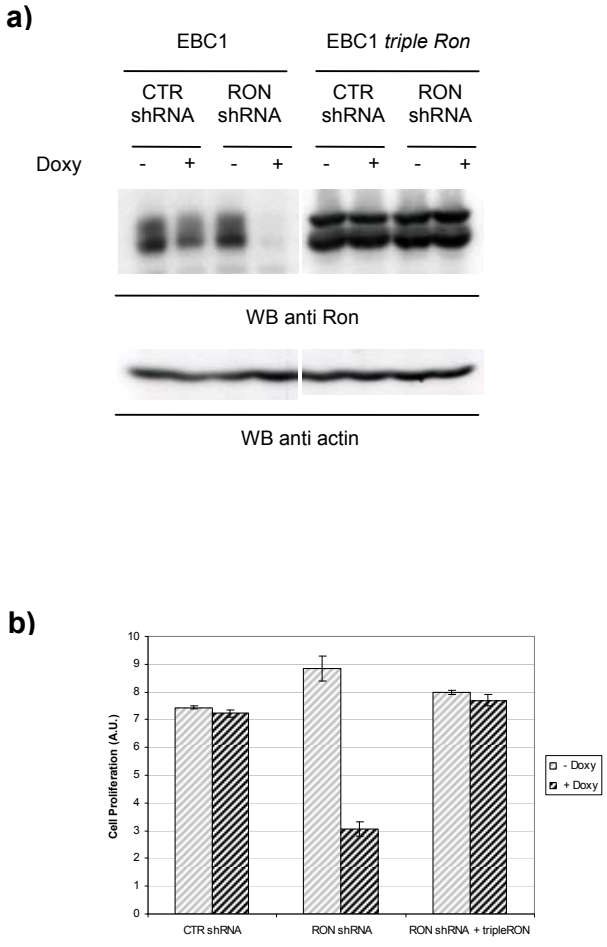
3. Eder, J.P., Vande Woude, G.F., Boerner, S.A., and LoRusso, P.M. 2009. Novel therapeutic inhibitors of the c-Met signaling pathway in cancer. *Clin. Cancer Res.* **15**:2207-2214.



Supplementary figure 2

Ligand stimulation

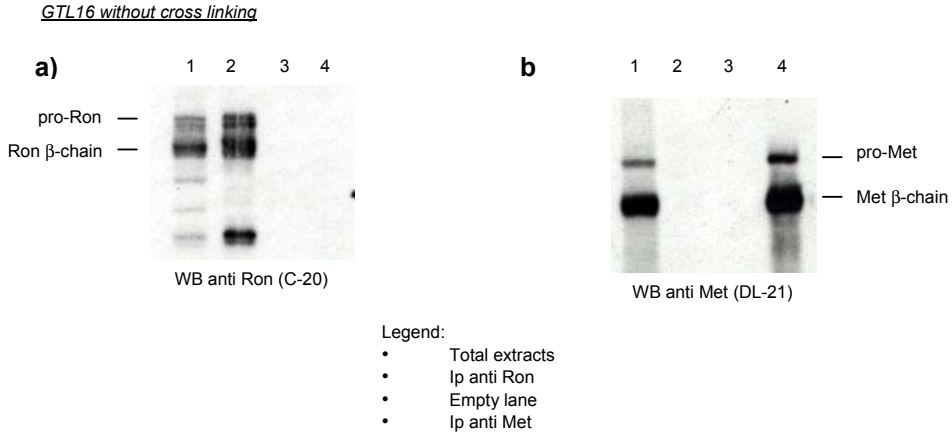
GTL16, starved for 48 hours in 0% serum (FBS) were subsequently treated for 2 hours with PHA-665752 (PHA) and then stimulated for 15 minutes with MSP, either 100 or 300ng/ml as indicated. (**a**) Cell lysates were either run as total extracts (30µg) and *Met* phosphorylation status checked probing the membranes with a specific anti phospho-*Met* (P-*Met*) antibody or immunoprecipitated with *Ron* antibody (800µg) and receptor phosphorylation status was checked probing the membranes with anti P-Tyr antibody. Membranes were then reprobed with anti *Met* and anti *Ron* antibodies respectively. *Actin* antibody was used as loading control when total lysates were run. It can be noted that, within the contest of *Met* oncogene addiction, in the absence of active *Met* (obtained by pharmacological inhibition) the loss of *Ron* phosphorylation is not reverted by its ligand MSP. (**b**) MSP capability to phosphorylate *Ron* was checked in T47D.



Supplementary figure 3

Rescue of *Ron* expression

To control for unwanted off-target effects while silencing *Ron* expression a 'rescue' experiment was performed by expressing a *RON* cDNA (*triple Ron*) harbouring three silent mutations which render the receptor refractory to specific shRNA silencing. (**a**) Western blot analysis of total cell lysates (80µg) of EBC1 cells transduced either with RON or with CTR shRNA viruses and then super-infected with *triple Ron* virus. As shown, *triple Ron* restored *Ron* expression 72 hours after doxycycline treatment (1mg/ml) EBC1. *Actin* was used as loading control. (**b**) Proliferation rates were checked in EBC1 upon *Ron* expression restoration: rescue of Ron exprespression restored proliferation rates in cells expressing RON shRNA in presence of doxycycline (1mg/ml) (Doxy). Error bars report standard deviations of two experiments performed in quadruplicate.



Supplementary figure 4

Antibodies specificity

Anti *Met* (DL-21) and anti *Ron* (c-20) antibodies specificity was tested. The experiment was performed in GTL16 WITHOUT cross linking (otherwise *Met* and *Ron* co-immunoprecipitate). Following Met immunoprecipitation (performed with DL-21) no bands can be detected probing the membranes with anti *Ron* antibody (c-20) and similarly following *Ron* immunoprecipitation (performed with c-20) no bands can be detected probing the membrane with anti *Met* antibody (DL-21).