NALSAR PROXIMATE EDUCATION
NALSAR UNIVERSITY OF LAW, HYDERABAD
P.G.DIPLOMA IN PATENTS LAW

2012-13

Supplementary Exams (December, 2013)

(Exploitation of Patents – Drafting, Specification & Patent Writing)

Time: 2 ½ hours. **TOTAL MARKS: 90**

INSTRUCTIONS TO CANDIDATES

1. **The questions to be interpreted as given and no clarification can be sought from the invigilator.**
2. **Do not draw or attache figures.**
3. **The claim drafting will carry 50 marks.**
4. **The rest of the specification will carry 40 marks.**
5. **Attempt only one choice – either Option A or Option B.**

Option A

Draft a Patent based on the information given by the inventor as below:

Inventor Disclosure

Zoya is a vivid enthusiast of cooking and also teaches cooking through television programmes. As a cooking enthusiast she is also particular of the kitchen tools used in such shows as she feels that the culinary skills and output depends on appropriate kitchen tools.

Among the many tools, the kitchen tool to peel the skin of vegetables and fruits are crucial for preparing the ingredients of the recipe. There are a number of kitchen tools that are available for peeling the skin of vegetables and fruits. There are peelers having first and second pairs of parallel knife members that can be spaced as per the diameter of the vegetable to be processed. There are other peelers which are patented which discloses a peeler for peeling fruits and vegetables comprising a plurality of rotatably driven peeling elements having predetermined axes of rotation that are generally horizontal and substantially parallel to one another. The peeling elements have a provision for engaging the peel of the fruits and vegetables. Also there is a patented tool for peeling asparagus where the device has a housing with a passage designed to permit a

stick of asparagus to be inserted. Inside the housing are several peeling blades, which are disposed in different directions of the passage.

Also there are non slip cutting boards with a rigid planar baseboard which is fixed a traction to provide support and the free flow of fluid underneath the cutting board and which provides enhanced traction to retard slippage of the cutting board during the cutting or support process. In addition, another patented tool describes a cutting board comprising a slab of polyethylene made as a unitary molding. The board includes a central cutting zone, which drains to a liquid sump in one corner of the board.

The patented tools in the market have a general design of existing peelers and cutting boards is to treat vegetables and fruits that are generally rigid such as carrots, potatoes, asparagus, apples etc. As for as Zoya is concerned these devices do not address the processing of fruits or vegetables that are soft as a result of boiling or roasting such as for example roasted peppers. A boiled or roasted vegetable or fruit may disintegrate to an undesirable form if it is placed between the sharp knives or blades of conventional peelers.

Fresh roasted pepper is a delicacy savored by many. However the cleaning of such roasted peppers prior to their consumption is a difficult task. On roasting, the pepper becomes soft and conventional handling such as placing the peppers in a bucket of water or under the faucet to remove their seeds, veins and skin can often lead to the pepper losing most of its flavorful juices. Such handling of roasted peppers can also cause the pepper to disintegrate into a pulp, which is undesirable.

Thus, Zoya felt for the need in the art for a device to skin, remove veins and deseed roasted vegetables and fruits such as roasted pepper. More specifically there is a need for a device that can perform all these functions without causing undesirable damage to the fruit or vegetable. After working on such a tool, Zoya approaches you to file a Patent for her new tool, which fulfills this long-standing need in the art and it discloses the following information

A cooked vegetable or fruit becomes soft and removal of skin, seeds and veins usually results in loss of flavorful juices and disintegration of the fruit or vegetable to a pulp. The instant invention is directed to a system that specifically overcomes such problems associated with processing whole cooked vegetables and fruits. The system can also be used to peel other food material such as fish, poultry and meat and raw fruits and vegetables.

It has an inclined board having an upper surface with a plurality of parallel ridges laterally disposed thereon adapted to hold a fruit or vegetable thereon. The board has a downwardly extending support member adapted to support the board in an inclined position when the board is placed on a surface and a hand tool having an upper end adapted for being held by hand and a lower end

downwardly inclined from the upper end and with a lower edge adapted to peel a fruit or vegetable placed on the inclined board.

Roasted eggplants and peppers are examples of vegetables that can be processed using this system. Specifically the system can be used to remove the skin, seeds and veins of roasted pepper such as for example roasted Bell or Banana peppers. The system may also be used to remove scales from fish or to peel poultry or meat.

BRIEF DESCRIPTION OF THE DRAWINGS

So that the matter in which the above-recited features, advantages and objects of the invention, as well as others, which will become clear, are attained and can be understood in detail, more particular descriptions of the invention are briefly summarized. The above may be better understood by reference to certain embodiments thereof, which are illustrated in the appended drawings. These drawings form a part of the specification. It is to be noted; however, that the appended drawings illustrate preferred embodiments of the invention and therefore are not to be considered limiting in their scope.

FIGS. 1A-1B show a system for peeling a vegetable or fruit. FIG. 1A shows an inclined and ridged board for holding the fruit or vegetable FIG. 1B shows a hand tool for removing the seeds, veins and skin from a fruit or vegetable that is placed and held against the ridges of the inclined board.

FIG. 2 illustrates the peeling of roasted pepper skin using the system described in

FIGS. 1A-1B.

Referring now to FIG. 1A, the flexible rectangular board 1 has a series of parallel upwardly inclined laterally disposed rectangular ridges 2 on the upper surface 3. The upper edge 4 of each ridge 2 is approximately 2 mm from the surface of the inclined board 1. A support member 5 extends downwardly from the upper edge 6 to hold the board 1 in an inclined position when the board is placed on a surface (not shown). The lower edge 7 of the board 1 rests on the surface when the board 1 is placed on a surface. The two side edges 8 and 9 of the board 1 are elevated above the surface when the board is placed on a surface. The board 1 has a perforation 10 to hang the board on a wall (not shown).

Referring now to FIG. 1B, the hand tool 11 has a rectangular upper end 12 for holding and a downwardly inclined lower end 13 extending from the upper end 12. The lower end 13 has a lower edge 14 adapted to peel food material (not shown) held on board 1 of FIG. 1A.

FIGURES

PART A

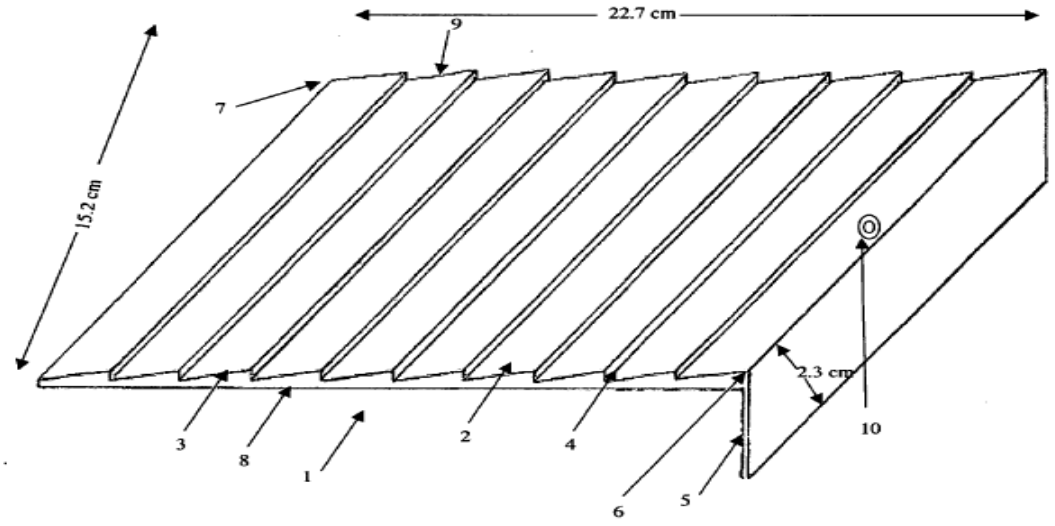


Fig. 1A

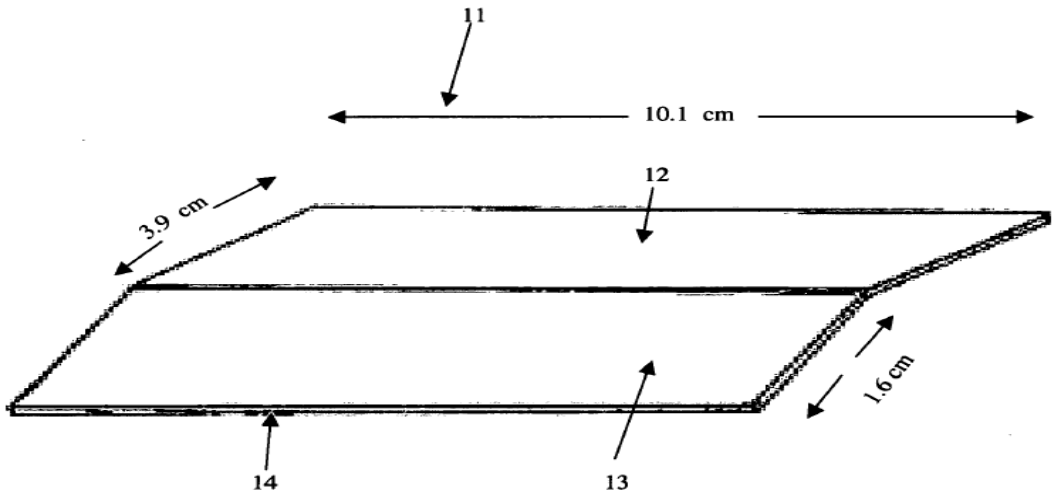


Fig. 1B

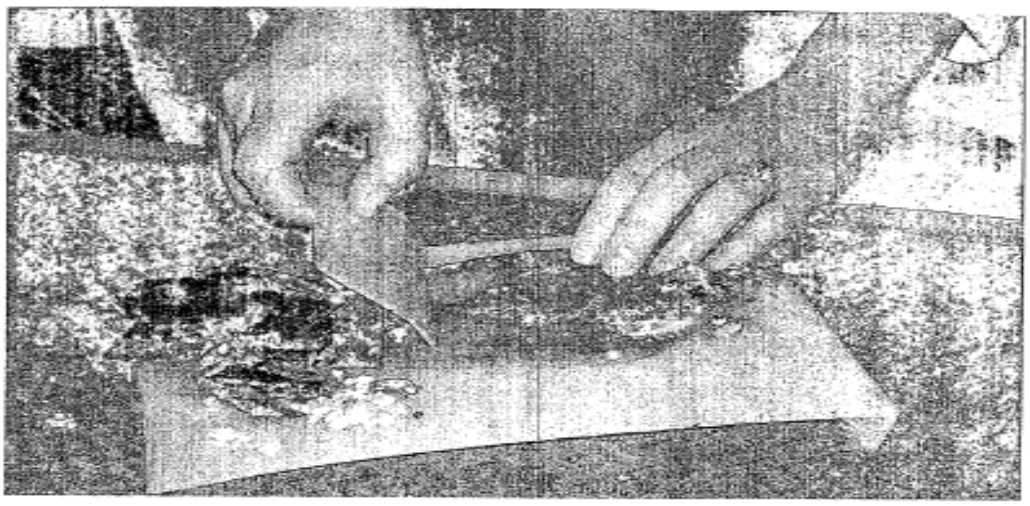


Fig. 2

Option B

Chidambaram a scientist working on treatment on Cancer approaches you with the following inventor disclosure to file for a patent. You are required to file a Patent based on the following disclosure:

Signal transduction proteins have increased importance in carcinogenesis and tumor formation and represent attractive targets for the development of novel anticancer therapeutics.

The Signal Transducer and Activator of Transcription (STAT) family of proteins are cytoplasmic transcription factors with important roles in mediating responses to cytokines and growth factors, including promoting cell growth and differentiation, and inflammation and immune responses (1,2). Normal STATs activation is initiated by the phosphorylation of a critical tyrosine residue upon the binding of cytokines or growth factors to their cognate receptors. The phosphorylation is induced by growth factor receptor tyrosine kinases, or cytoplasmic tyrosine kinases, including Janus kinases or the Src family kinases. While pre-existing dimers have been detected (3,4), phosphorylation is observed to induce dimerization between two STAT monomers through a phosphotyrosine interaction with the SH2 domain. In the nucleus, active STAT dimers bind to specific DNA-response elements in the promoters of target genes and regulate gene expression.

It is now well established that aberrant activation of the member of the family, Stat3 contributes to malignant transformation and tumorigenesis. Aberrant Stat3-mediated oncogenesis and tumor formation is due in part to the transcriptional upregulation of critical genes, which in turn lead to dysregulation of cell growth and survival, and the promotion of angiogenesis (2, 5-11) and tumor immune-tolerance (12, 13). Thus, targeting of aberrant Stat3 signaling would provide a novel strategy for treating the wide variety of human tumors that harbor abnormal Stat3 activity.

The critical step of dimerization (14) between two monomers within the context of STAT activation presents an attractive strategy to interfere with Stat3 activation and functions and this approach has been exploited in prior work (15-25). Leading agents from those earlier studies have been explored for rational design in conjunction with molecular modeling of the binding to the Stat3 SH2 domain(18, 19), per the X-ray crystal structure of the Stat3 homodimer (26). One of those leads, S3I-201 (18) had previously been shown to exert antitumor effects against human breast cancer xenografts via mechanisms that involve the inhibition of aberrant Stat3.

In the present study, key structural information from the computational modeling of S3I-201 bound to the Stat3 SH2 domain facilitated the design of

novel analogs of which S3I-201.1066 and S3-201.2096 show improved Stat3-inhibitory activity. Both S3I-210.1066 and S3I-201.2096 inhibit Stat3 activity with IC.sub.50 values of 35 and 45 .mu.M, respectively. This disclosure presents evidence that S3I-201.1066 interacts with the Stat3 protein and disrupts Stat3 binding to its cognate pTyr peptide of receptors. Furthermore, S3I-201.1066 induces antitumor cell effects selectively in malignant cells harboring aberrant Stat3 and antitumor response in vivo in human breast xenografts.

With the foregoing in mind, the present invention advantageously provides a useful expansion of several prior studies that have provided the proof-of-concept for the therapeutic effects of Stat3 inhibitors in human tumors. The molecular modeling of the phosphotyrosine (pTyr)-SH2 domain interaction in Stat3:Stat3 dimerization, combined with in silico structural analysis of the previously reported Stat3 dimerization disruptor, S3I-201, has furnished a diverse set of analogs.

BRIEF DESCRIPTION OF THE DRAWINGS

Some of the features, advantages, and benefits of the present invention having been stated, others will become apparent as the description proceeds when taken in conjunction with the accompanying drawings, presented for solely for exemplary purposes and not with intent to limit the invention thereto, and in which:

FIG. 1(A-C), illustrates structures of (A) S3I-201, (B) S3I-201.1066 and (C) S3I-201.2096; D and E, GOLD docking of (D) S3I-201 (green), and (E) S3I-201.1066 (yellow) and S3I-201.2096 (green) to the SH2 domain of Stat3; arrow denotes potential binding sub-pocket;

FIG. 2 shows effects of S3I-201.1066 and S3I-201.2096 on the activities of STATs, Src, Jak1, Shc, and Erks. (A) Nuclear extracts of equal total protein containing activated Stat1, Stat3, and/or Stat5 were pre-incubated with or without (i), (iii) and (iv) S3I-201.1066 or (ii) S3I-201.2096 for 30 min at room temperature prior to the incubation with the radiolabeled hSIE probe that binds Stat1 and Stat3 or the MGFe probe that binds Stat5 and subjecting to EMSA analysis; (B) Nuclear extracts of equal total protein prepared from malignant cells following 24-h treatment with or without S3I-201.1066 were subjected to in vitro DNA-binding assay using the radiolabeled hSIE probe and analyzed by EMSA; (C) Cytosolic extracts of equal total protein were prepared from 36-h S3I-201.1066-treated or untreated NIH3T3/v-Src fibroblasts that stably express the Stat3-dependent luciferase reporter (pLucTKS3) and analyzed for luciferase activity using a luminometer; and (D) SDS-PAGE and Western blotting analysis of whole-cell lysates of equal total protein prepared from S3I-201.1066-treated or untreated NIH3T3/v-Src and Panc-1 cells probing for pY705Stat3, Stat3, pY416Src, Src, pJak1, Jak1, pShc, Shc, pErk1/2 and Erk1/2. Positions of

STATs:DNA complexes or proteins in gel are labeled; control lanes (0) represent nuclear extracts treated with 0.05% DMSO, or nuclear extracts or whole-cell lysates prepared from 0.05% DMSO-treated cells. Data are representative of 3-4 independent determinations. ** -<0.01;

FIG. 3 depicts studies of the interaction of S3I-201.1066 with Stat3 or the Stat3 SH2 domain. (A) EMSA analysis of in vitro binding of Stat3 to the radiolabeled hSIE probe using nuclear extracts containing activated Stat3 pre-incubated with 0-100 .mu.M S3I-201.1066 in the presence or absence of increasing concentrations of purified His-tagged Stat3 SH2 domain; (B) Surface Plasmon Resonance analysis of the binding of (i) GYLPQTV-NH2 (unphosphorylated, high affinity gp-130 peptide), (ii) GpYLTQTV-NH2 (phosphorylated), or (iii) small-molecule S3I-201.1066 as analyte to the purified His-tagged Stat3 immobilized on HisCap Sensor Chip; and (C) Fluorescence Polarization assay of the binding to the 5carboxyfluorescein-GpYLPQTV-NH2 probe of (i) increasing concentration of purified His-Stat3 or (ii) a fixed amount of purified His-Stat3 (150 nM) in the presence of increasing concentrations of S3I201.1066. Stat3:DNA complexes in gel are shown, control (-) lane or zero (0) represent 0.05% DMSO. Data are representative of 2-4 independent determinations;

FIG. 4 shows the effect of S3I-201.1066 on the colocalization or association of Stat3 with EGF receptor and on Stat3 nuclear translocation. (A) Immunofluorescence imaging/confocal microscopy of Stat3 colocalization with EGFR and Stat3 nuclear localization in EGF-stimulated (1 g/ml; 10 min) NIH3T3/hEGFR pre-treated with or without 50 .mu.M S3I-201.1066 for 30 min; or (B) Immunoblotting analysis of (i) EGFR immunecomplex (upper panel) or whole-cell lysates (lower panel) from S3I201.1066-treated Panc-1 and MDA-MB-231 cells, or (ii) immunecomplexes of EGFR (upper panel) or Stat3 (lower panel) treated with the indicated concentrations of S3I-201.1066 and probing for EGFR, Stat3, Shc, Grb 2, or Erk1/2MAPK. Data are representative of three independent studies;

FIG. 5 indicates that S3I-201.1066 suppresses viability, growth and survival of malignant cells that harbor persistently-active Stat3 Human breast (MDA-MB-231) and pancreatic (Panc-1) cancer cells, the normal mouse fibroblasts (NIH3T3) and their v-Src transformed (NIH3T3/v-Src) or v-Ras transformed (NIH3T3/v-Ras) counterparts, mouse thymic epithelial stromal cells (TE-71), Stat3 null mouse embryonic fibroblasts (Stat3-/-), and the normal human pancreatic duct epithelial cells (HPDEC) were treated once or untreated with 30-100 M S3I-201.1066 for 24-144 h. Cells were (A) assayed for viability using CyQuant cell proliferation kit; IC.sub.50 values were derived from graphical representation; (B) harvested at each 24-h period following treatment and viable cells counted by trypan blue exclusion with phase-contrast microscopy; or (C) allowed to culture until large colonies were visible, which were stained with crystal violet and enumerated. Values are the mean and S.D. of 3-4 independent determinations. p values, * -<0.05, and ** -<0.01;

FIG. 6 demonstrates that S3I-201.1066 blocks Stat3-dependent malignant transformation and inhibits the migration of malignant cells harboring aberrant Stat3. (A) Viral Src-transformed mouse fibroblasts (NIH3T3/v-Src) and counterpart transformed by v-Ras (NIH3T3/v-Ras) growing in soft-agar suspension were treated with or without 30-100 .mu.M S3I-201.1066 every 2-3 days until large colonies were visible, which were stained with crystal violet and enumerated; (B) Wound healing assay for effect on cell migration in which human breast (MDA-MB-231) and pancreatic (Panc-1) cancer cells, and the v-Src transformed mouse fibroblasts (NIH3T3/v-Src) and counterparts transformed by v-Ras (NIH3T3/v-Ras) were treated with or without 30-80 .mu.M S3I-201.1066 for 12-24 h and allowed to migrate into the denuded area. Cell migration was visualized at 10.times. magnification by light microscopy and cells that migrated into the denuded area counted and plotted against the concentration of S3I-201.1066. Values are the mean and S.D. of 3 independent determinations. p values, * -<0.05, and ** -<0.01.

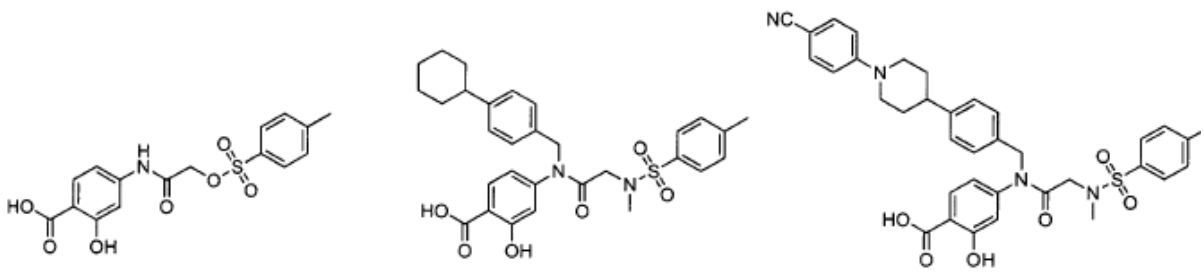
FIG. 7 shows that S3I-201.1066 suppresses c-Myc, Bcl-xL, MMP-9 and VEGF expression. SDS-PAGE and Western blotting analysis of whole-cell lysates prepared from the human breast cancer MDA-MB-231 and pancreatic cancer Panc-1 cells untreated (DMSO, control) or treated with 80-100 .mu.M S3I-201.1066 for 48 h and probing with anti-Myc, Bcl-xL, MMP-9, VEGF or .beta.-actin antibodies. Positions of proteins in gel are shown. Data are representative of 3 independent determinations; and

FIG. 8 shows that S3I-M2001 inhibits growth of human breast tumor xenografts. Human breast (MDA-MB231) tumor-bearing mice were given S3I-201.1066 (3 mg kg-1) or vehicle (0.1% DMSO in PBS) i.v. every 2 or 3 days. Tumor sizes, measured every 2 or 3 days, were converted to tumor volumes and plotted against treatment days; Values are the mean and S.D. from replicates of 12 tumor-bearing mice in each group. *<0.05.

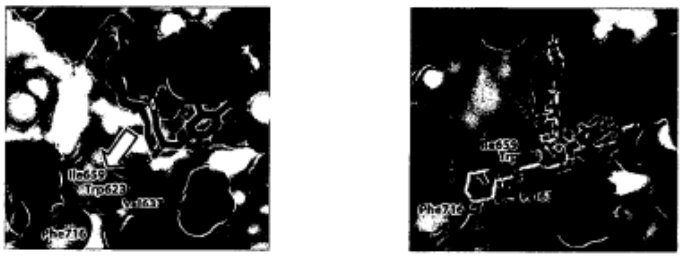
FIGURES

PART B

Fig. 1



A S3I-201 B S3I-201.1066 C S3I-201.2096



D S3I-201 E Green = SF-2-096
Yellow = SF-1-066

Fig. 2

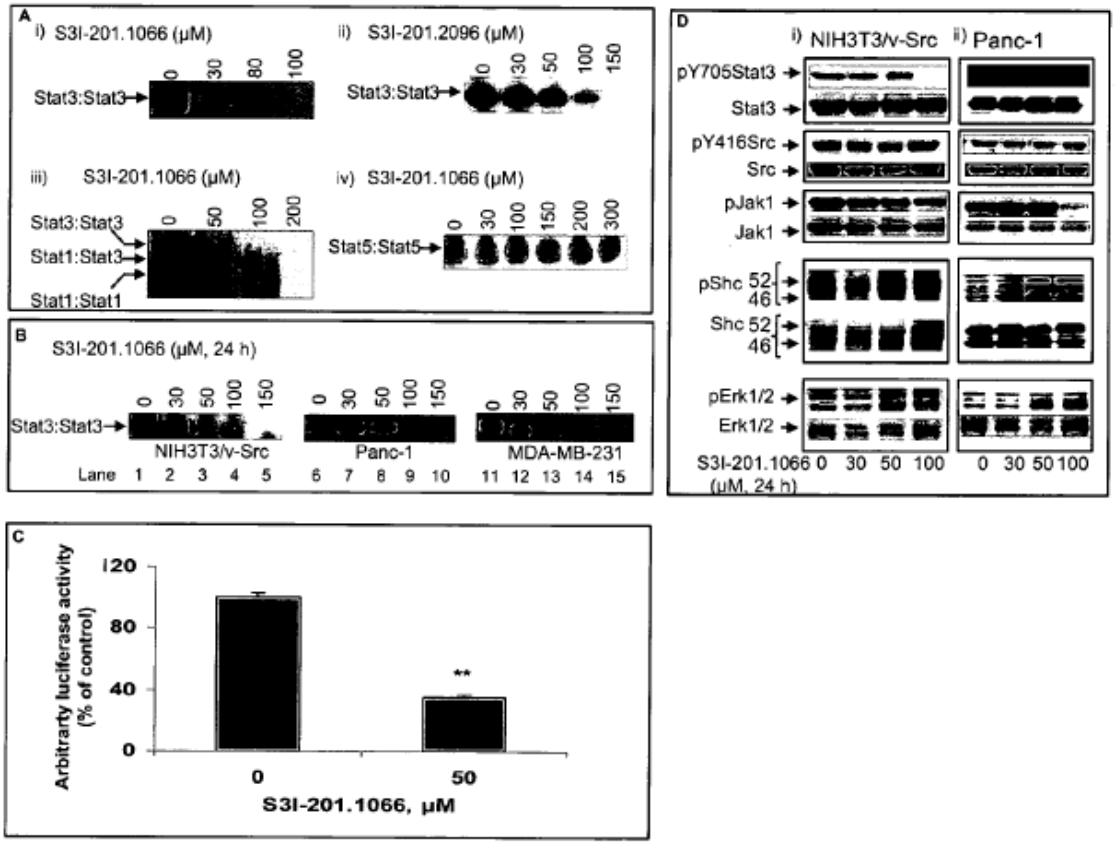


Fig. 3

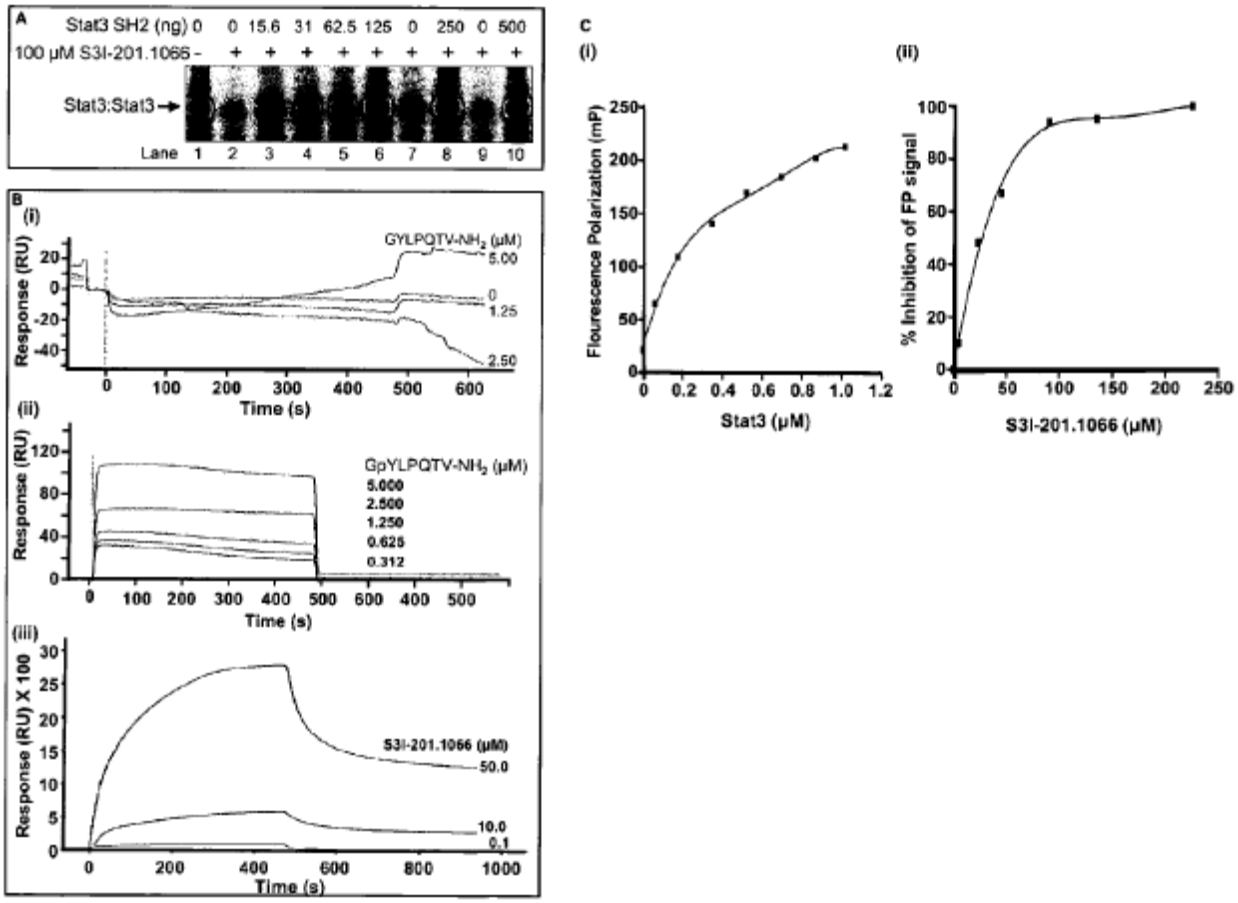

A
Stat3 SH2 (ng) 0 0 15.6 31 62.5 125 0 250 0 500
100 μM S3I-201.1066 - + + + + + + + + +
Stat3:Stat3
Lane 1 2 3 4 5 6 7 8 9 10
B
(i)
Response (RU)
GYLPQTV-NH2 (μM)
5.00
0
1.25
2.50
Time (s)
(ii)
Response (RU)
GpYLPQTV-NH2 (μM)
5.000
2.500
1.250
0.625
0.312
Time (s)
(iii)
Response (RU) X 100
S3I-201.1066 (μM)
50.0
10.0
0.1
Time (s)
C
(i)
Flourescence Polarization (mP)
Stat3 (μM)
(ii)
% Inhibition of FP signal
S3I-201.1066 (μM)

Fig. 4

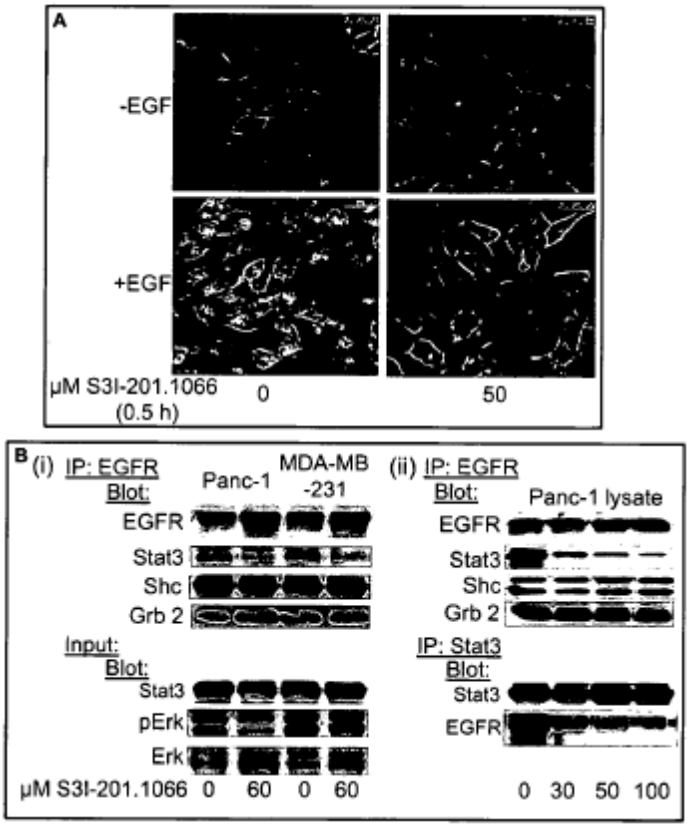

A
-EGF
+EGF
μM S3I-201.1066 0 50
(0.5 h)
B
(i) IP: EGFR
Blot:
Panc-1
MDA-MB -231
EGFR
Stat3
Shc
Grb 2
Input:
Blot:
Stat3
pErk
Erk
μM S3I-201.1066 0 60 0 60
(ii) IP: EGFR
Blot:
Panc-1 lysate
EGFR
Stat3
Shc
Grb 2
IP: Stat3
Blot:
Stat3
EGFR
0 30 50 100

Fig. 5

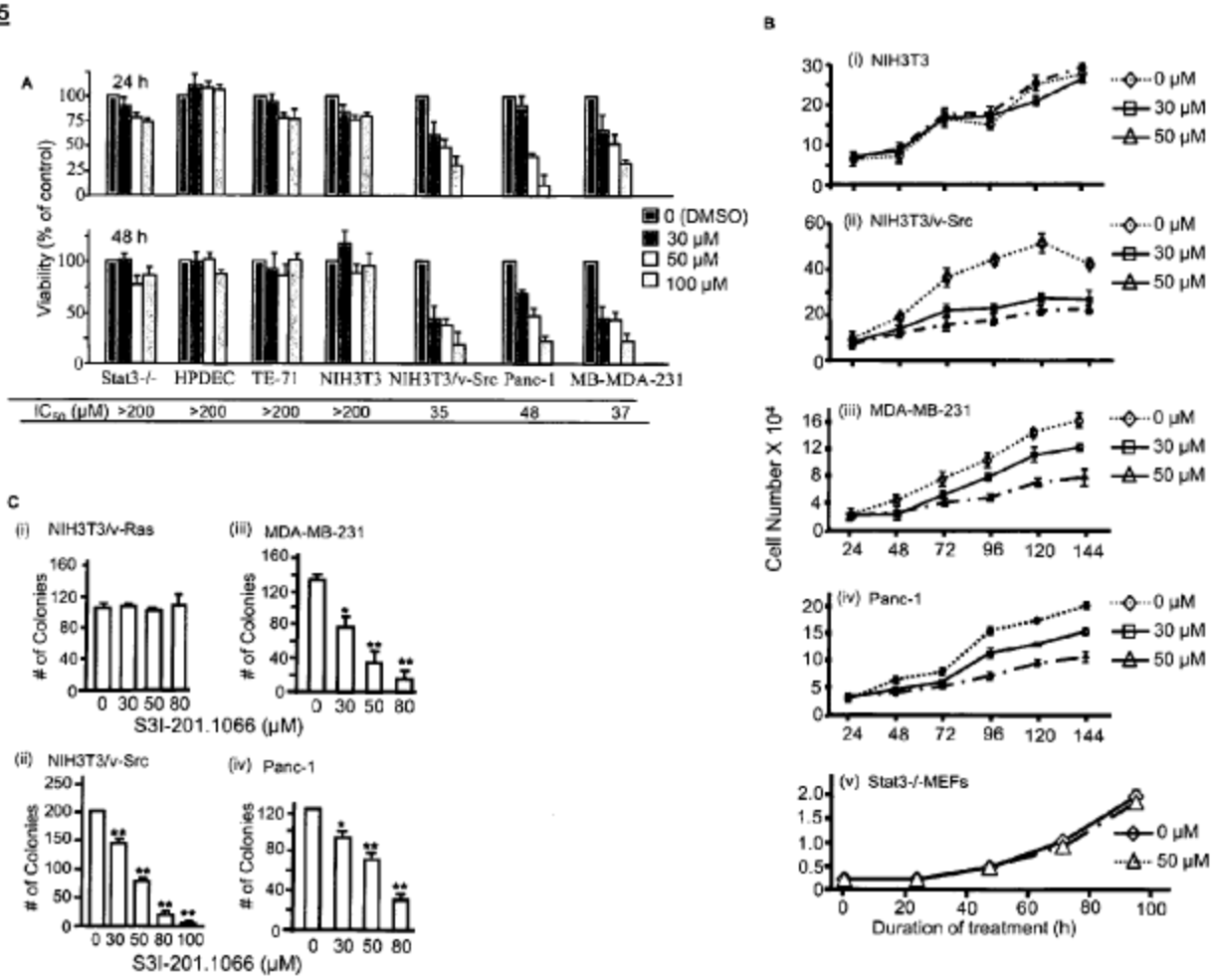

A
24 h
48 h
Viability (% of control)
0 (DMSO)
30 μM
50 μM
100 μM
Stat3-/-
HPDEC
TE-71
NIH3T3
NIH3T3/v-Src
Panc-1
MB-MDA-231
IC50 (μM) >200 >200 >200 >200 35 48 37
B
(i) NIH3T3
(ii) NIH3T3/v-Src
(iii) MDA-MB-231
(iv) Panc-1
(v) Stat3-/-MEFs
Cell Number X 10⁴
Duration of treatment (h)
C
(i) NIH3T3/v-Ras
(ii) NIH3T3/v-Src
(iii) MDA-MB-231
(iv) Panc-1
# of Colonies
S3I-201.1066 (μM)

Fig. 6

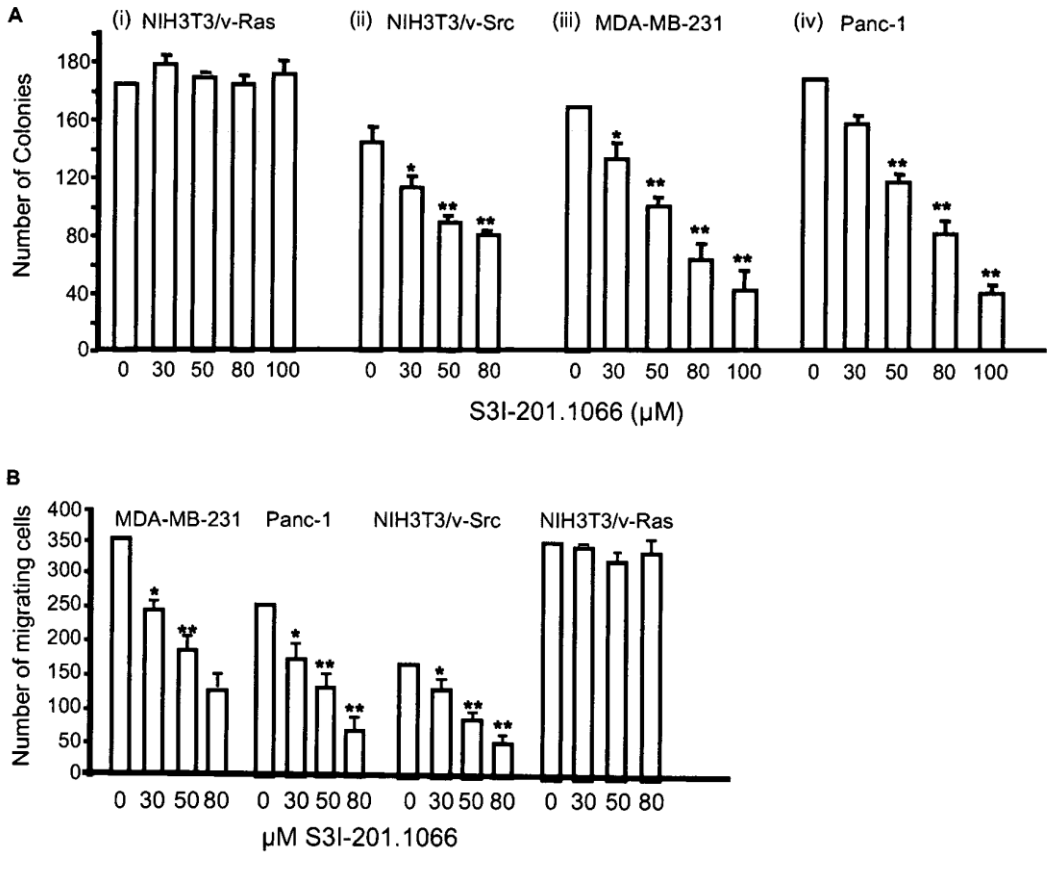

A
(i) NIH3T3/v-Ras
(ii) NIH3T3/v-Src
(iii) MDA-MB-231
(iv) Panc-1
Number of Colonies
S3I-201.1066 (μM)
B
MDA-MB-231
Panc-1
NIH3T3/v-Src
NIH3T3/v-Ras
Number of migrating cells
μM S3I-201.1066

Fig. 7

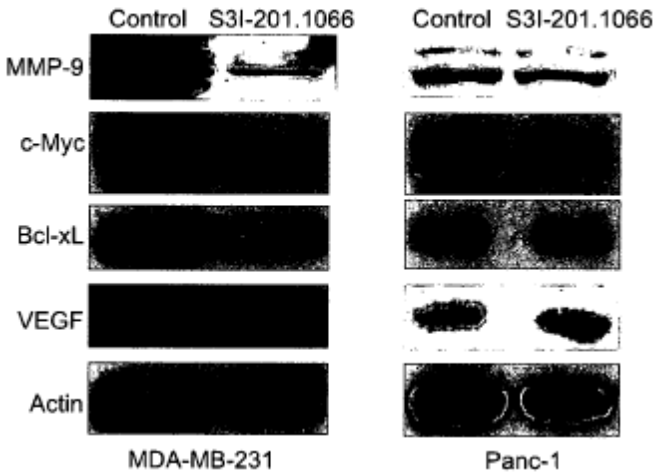
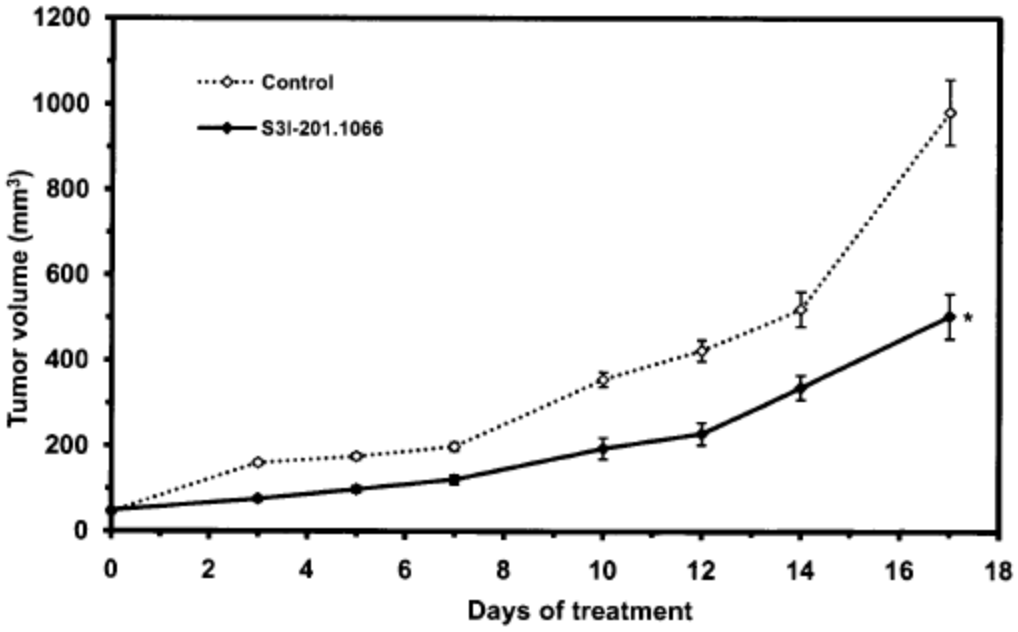

Control
S3I-201.1066
Control
S3I-201.1066
MMP-9
c-Myc
Bcl-xL
VEGF
Actin
MDA-MB-231
Panc-1

Fig. 8


Control
S3I-201.1066
Tumor volume (mm3)
Days of treatment
0
200
400
600
800
1000
1200
0
2
4
6
8
10
12
14
16
18
*