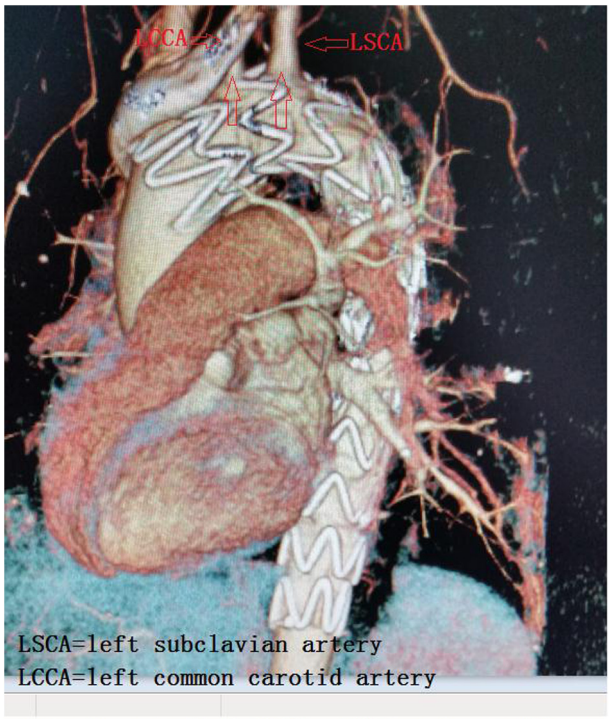

Fig 7. Computed tomography angiography follow-up

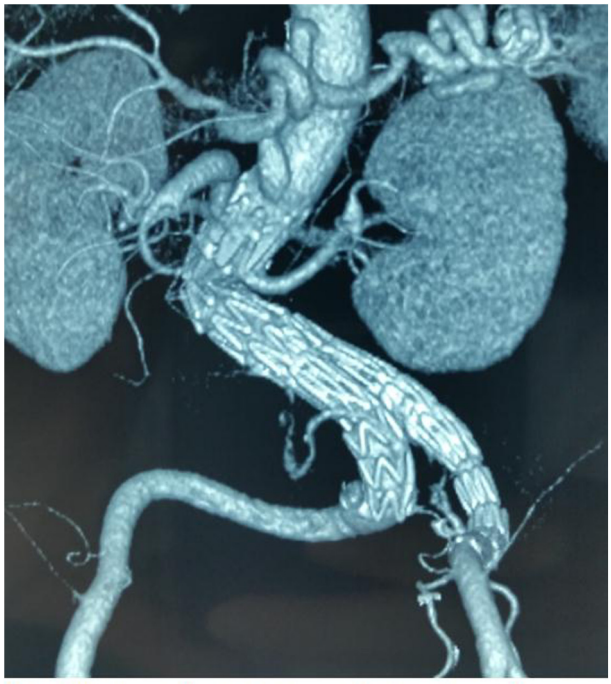

Fig 8. Computed tomography angiography follow-up

BASIC SCIENCE, ANIMAL MODELS AND PRECLINICAL STUDIES (TCTAP A-048 TO TCTAP A-053)

TCTAP A-048

Neural Network Model as the Multidisciplinary Team Member in Clinical Decision Support to Avoid Medical Mistakes (aLYNX concept)

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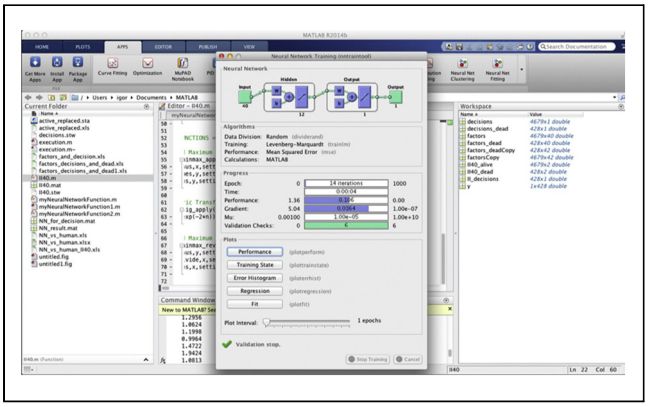
BACKGROUND The feedback is the essential part of any system. aLYNX concept is an idea to use some fuzzy logic algorithm, for example, a neural network model in decision-making system to avoid possible mistakes in a choice between PCI and CABG.

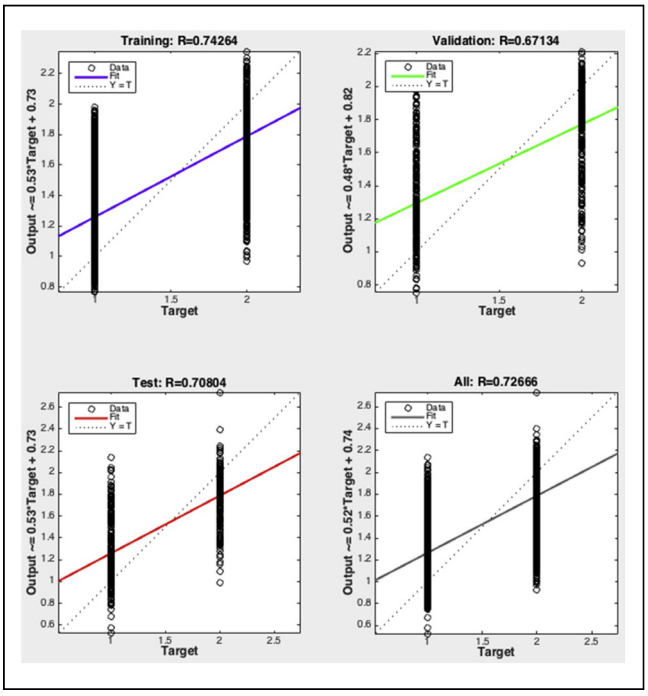
METHODS aLYNX system contains:

first - a registry with parameters, decisions, and late results;
second - machine learning process based on successful cases registry data;
third - the use of the machine learning results as the adviser.

Objective: To show a possibility to build a mathematic model as an adviser for making a decision between CABG and PCI based on the experience of 5107 patients.

RESULTS The neural network was trained by 4,679 patients who achieved 5-year survival. Among them, 2,390 patients underwent PCI and 2289 CABG. After training, the correlation coefficient (r) of the network was 0.74 for training, 0.67 for validation, 0.71 for test and 0.73 for a total. Simulation of the neural network function has been performed after training in the two groups of patients with a known 5-year outcome. The disagreement rate was significantly higher in the dead patient group than that in the survivor group between a neural network model and heart team [16.8% (787/4679) vs. 20.3% (87/428), P=0.065)].





CONCLUSION aLYNX concept shows the possibility to use a neural network model in decision-making to remind the doctors to review tactics once more in selected cases. Such system should include registry with significant factors, decisions, and results; machine learning process based on the registry data; using the machine learning results as the adviser.

TCTAP A-049

Cardio Protective Effect of Substance P in a Porcine Model of Acute Myocardial Infarction

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BACKGROUND Substance P (SP) is known to reduce inflammatory reaction and induce mobilization of stem cells, suggesting a potential benefit of reducing ischemia-reperfusion injury and infarct size. We reported the cardio protective effect of SP in a rat and mouse model. We assessed a cardio protective effect of SP in a porcine model of acute myocardial infarction (MI).

METHODS A total of 16 pigs were randomly allocated to group 1 (substance P, n=8) and group 2 (placebo, n=8). Acute MI was induced by occlusion of the left anterior descending artery with a 3.0 mm balloon catheter for 50 minutes. Five minutes before reperfusion, substance P (5 nmol/kg) and normal saline were administered intravenously in group 1 and 2, respectively. Two-dimensional echocardiography and myocardial perfusion single photon emission computed tomography (SPECT) with technetium-99 m sestamibi were performed at 1 week and 4 weeks after the procedure to assess left ventricular (LV) function and infarct size. At 4 weeks, the pigs underwent follow-up coronary angiography and were sacrificed for histomorphometric infarct size assessment.

RESULTS Baseline LV ejection fraction (LVEF), LV end-diastolic and end-systolic volumes were similar between 2 groups. LVEF at 1 week was significantly higher in group 1 than group 2 (37.9 ± 4.6% vs. 29.4 ± 3.2%, p=0.001). LVEF at 4 weeks was not different between the groups (41.1 ± 8.8% vs. 38.0 ± 4.4%, p=0.427). The number of defect segments and the magnitude of total perfusion defect on SPECT were lower in group 1, compared to group 2 at 1 week (0.5 ± 0.8 vs. 2.1 ± 2.3, p=0.118 and 15.4 ± 8.6% vs. 23.6 ± 18.5%, p=0.313, respectively) and at 4 weeks (0.5 ± 0.8 vs. 1.1 ± 1.1, p=0.197 and 13.3 ± 10.3% vs. 14.7 ± 12.0%, p=0.803, respectively). Pathologic infarct size (% LV) was significantly lower in group 1, compared to group 2 (2.4 ± 2.3% vs. 5.7 ± 2.5%, p=0.020).

CONCLUSION In a porcine model of acute MI, substance P improved LVEF early post-MI and reduced infarct size at 4 weeks. SP might be used for prevention of IR injury in MI.

TCTAP A-050

G2, a Hirsutine Analogue, Could Exert Endothelium-dependent Vasodilatory Effects in Vitro and Endothelial Protection in Vivo

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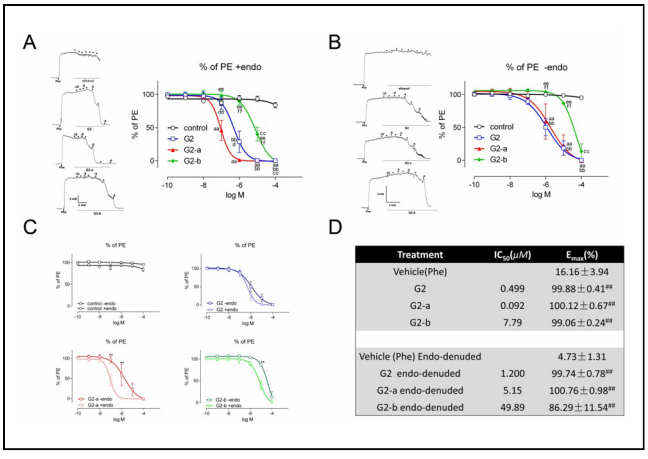
BACKGROUND Hirsutine, a compound extracted from *Uncaria rhynchophylla*, has been proven to be able to exert vasodilatory effects and cardioprotective effects on hypoxic neonatal rat cardiomyocytes. In order to acquire a deeper insight into the pharmacological functions and clinical applications of hirsutine, we synthesized its analogue, G2, to serve as our drug candidate for the treatment of microvascular dysfunction.

METHODS Superior mesenteric arteries isolated from male Sprague-Dawley rats was mounted in myograph chambers (Danish Myo Technology, Aarhus, Denmark) for further functional study. G2, including the enantiomers G2-a and G2-b in G2, was separately subjected to superior mesenteric arteries from rats pre-exposed to 60 mM KCl or 10 μM phenylephrine to confirm their vasorelaxant effects. Rat diabetic model was also established to assess the *in vitro* vasodilatory effect of G2. G2 was also subjected to SD diabetic rats for *in vivo* measurement of endothelium protection and histological assessment.

RESULTS G2 and its enantiomers G2-a and G2-b could stimulate apparent vasodilatory effects on KCl and phenylephrine pre-treated mesenteric arteries. Meanwhile, the G2-a (IC_{50}=0.092 μM) was 100 fold and 10 fold stronger in vasodilation than the enantiomer G2-b (IC_{50}=7.9 uM) and the racemate G2 (IC_{50}=0.499 μM) respectively. Endothelium denudation could reduce G2, G2-a, and G2-binduced vasorelaxant effects. Diabetes triggered endothelium dysfunction and L-NAME pretreatment could lead to similar vasorelaxant effect reduction, which meant that G2-evoked vasodilatory effect was endothelium-dependent. G2 subjected to diabetic rats could attenuate diabetes-damaged acetylcholine-induced endothelium-dependent relaxations. Immunohistochemical staining and western blot showed that eNOS was upregulated and no concentration was increased in diabetic vessels.

CONCLUSION G2, and its enantiomers G2-a and G2-b could exert endothelium-dependent vasodilatory effects *in vitro* through and endothelial protection *in vivo*. Meanwhile, the effectiveness of G2-a and G2-b was highly distinguishing in wire myograph assay.



Treatment	$IC_{50}(\mu M)$	E_{max}(%)
Vehicle(Phe)		16.16±3.94
G2	0.499	99.88±0.41##
G2-a	0.092	100.12±0.67##
G2-b	7.79	99.06±0.24##
Vehicle (Phe) Endo-denuded		4.73±1.31
G2 endo-denuded	1.200	99.74±0.78##
G2-a endo-denuded	5.15	100.76±0.98##
G2-b endo-denuded	49.89	86.29±11.54##