读书报告

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miR-122-5p as a plasma biomarker of liver injury in fish exposed to microcystin-LR

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目 录

研究背景

　　长期以来，　AST和ALT作为肝脏损伤的敏感标志物一直倍受临床医生青睐。诚然，二者在肝脏损伤性疾病的诊断、病情评估疗效评价中有着举足轻重的作用，但其缺陷也显而易见：特异性太差。众所周知，AST和ALT并不是肝脏特异性的标志物，二者增高也见于肾脏损伤、骨骼肌损伤等情况。尽管人们从蛋白质组学和转录组学的角度探索肝脏标志物的努力从未中断，但多数时候事与愿违，探索标志物的脚步却屡屡受阻。
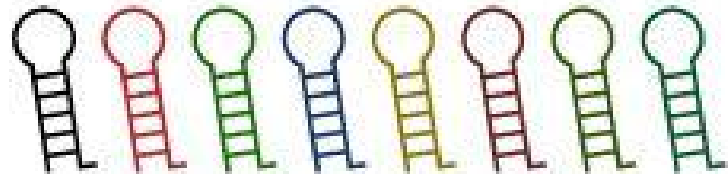
　　microRNA是近年来新发现一类非编码RNA分子，因其能介导目的基因的转录后调控机制而倍受学界关注。同时，由于microRNA的表达具有良好的组织特异性，因此可能是一种潜在的疾病标志物。
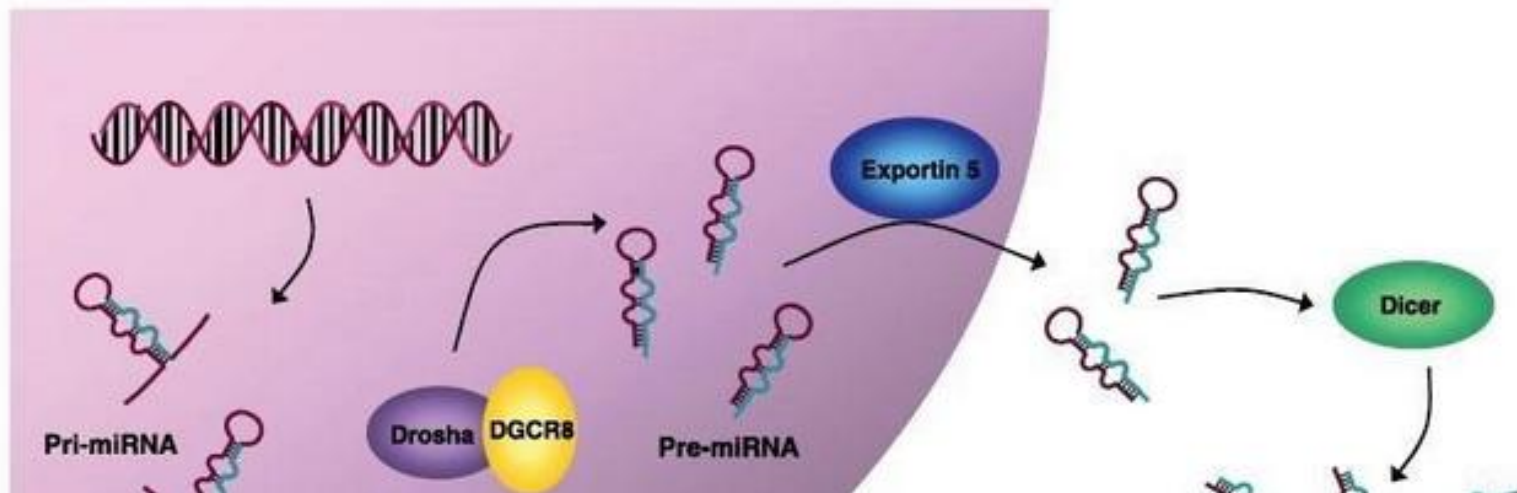
疾病检测新指标
miRNA
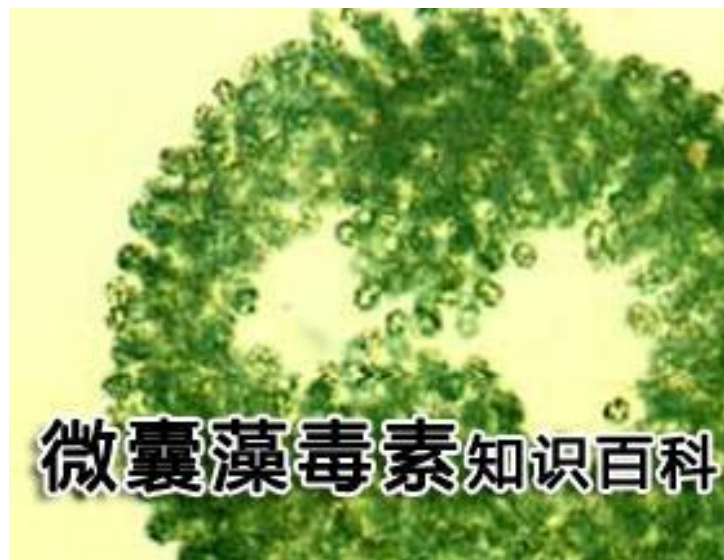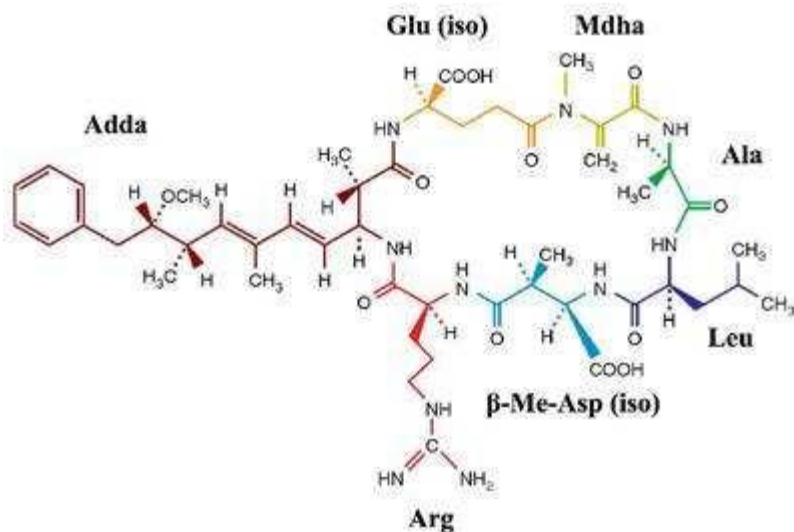
研究背景

miR-122：新型肝脏损伤标志物

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研究背景

微囊藻毒素

　　微囊藻毒素(Microcystin，MC)是一类具有生物活性的环状七肽化合物，为分布最广泛的肝毒素。主要由淡水藻类铜绿微囊藻(Microcystis aeruginosa)产生。具有相当高的稳定性。它能够强烈抑制蛋白磷酸酶的活性，还是强烈的肝脏肿瘤促进剂。

重楼皂苷对微囊藻毒素致小鼠肝损伤保护作用的组织学... 百度学术

杨黎江，路斌，沈放 - 《昆明学院学报》 - 2014

试验用重楼薯蓣皂苷(SY)和偏诺皂苷(PN)对微囊藻毒素浸染的小鼠进行连续灌胃,并通过对小鼠肝脏进行石蜡包埋、制片和HE染色,观察小鼠肝组织的显微结构,目的在于研究重...

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三峡库区水环境微囊藻毒素污染的人群肝损伤/肝癌... 百度学术

舒为群，陈济安，蒲朝文 - 海峡两岸毒理学研讨会大会 - 2013

正三峡水库是世界上最大的半封闭性水体,库区人口达三千万。我们的研究显示,库区内长江干流水及城市自来水的微囊藻毒素(MCs)尚在WHO及国标限值1.0μg/L以内,但部分乡镇的...

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JNK在微囊藻毒素诱导的小鼠氧化肝损伤中的作用机制... 百度学术

翁丹 - 南京大学 - 2007

微囊藻毒素(Microcystins,MCs)是由淡水微囊藻 产生的一类次生代谢物毒素,结构为环状七肽。MCs的毒性主要表现为肝毒性,此外还包括肾毒性、胃肠道毒性、免疫毒性、神经...

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谷胱甘肽转移酶基因多态性在微囊藻毒素致人群肝损伤... 百度学术

李砚，陈济安，赵清 - 《第三军医大学学报》 - 2010 - 被引量:3

目的探讨谷胱甘肽转移酶(glutathioneS-transferase,GST)M1(GSTM1)和T1(GSTT1)基因多态性在微囊藻毒素(microcystins,MCs)致人群肝损伤发生中的作用。方法在重庆涪陵区...

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微囊藻毒素肝损伤 相关论文(共39篇) 百度学术

  三峡库区水环境微囊藻毒素污染的人群肝损伤/肝癌风险... 中国毒理学会...   被引:1

  微囊藻毒素暴露及谷胱甘肽基因多态性与儿童肝损伤关系 第三军医大学   被引:1

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Despite the potential application of circulating microRNAs as biomarkers of tissue injury in mammals, there is still a lack of research on the use of miRNAs to diagnose liver damage in nonmammalian species such as fish.

真白鲑

Coregonus lavaretus

真白鲑，*Coregonus lavaretus* （Linnaeus, 1758），鲑科白鲑属的一种鲑鱼。体长73厘米，重量10公斤，原产于瑞士日内瓦湖和法国边境布尔歇湖，后引进至东欧和俄罗斯。常见于大型淡水湖泊，无迁徙习性，以昆虫幼虫和甲壳类动物为主食。每年的12月份在近岸浅滩处产卵，通常在夜间进行。

　　由于白鲑鱼适合青海省低温冷水水域生长，且生长速度快、品质好，因此在青海省的部分水库已开展了规模化的网箱养殖，并在新疆、黑龙江等省区得到推广。

Therefore, in this study, we selected four abundant liver miRNAs, which have been implicated in various biological processes and considered previously as biomarkers of liver injury in mammals。

Table 1 Details of selected microRNAs of this study. The miRNA nomenclature followed the miRBase v. 21 (ssa; *Salmo salar*)

miRNA	miRNA sequence	Putative biological process[a]	miRNA reference
ssa-miR-122-5p	uggagugugacaaugguguuug	Fatty-acid metabolism, maintenance of adult liver phenotype	MIMAT0032301
ssa-miR-148a-3p	ucagugcauuacagaacuuugu	Promotes the hepatospecific phenotype, tumour suppressor	MIMAT0032380
ssa-miR-92a-3p	uauugcacuugucccggccugu	Cell proliferation, angiogenesis promoter	MIMAT0032708
ssa-let-7c-5p	ugagguaguagguuguaugguu	Signal transduction	MIMAT0032265

[a]Based on the literature review; see text for details.

材料和方法

实验用鱼

Coregonus lavaretus
98.8 +8.5 g mean weight,
24.0 +0.7 cm mean length

养殖管理

The fish were acclimated for 2 weeks at 10 °C. During the acclimation period, the whitefish were fed four times a day . After acclimatization, the fish were deprived of food for 2 days, then anaesthetized by immersion in etomidate solution prior to injection.

实验设计

Fifteen (Exposed) whitefish individuals received single intraperitoneal injections of MC-LR,
11 control fish were injected with an equal volume of saline solution alone.

材料和方法

1.Fish exposure to MC-LR

2.Collection of fish plasma samples

3.Total RNA extraction and reverse transcription
using the modified stem-loop method

4.microRNAs expression analysis using real-time
PCR

5.Statistical analysis

Gross observations

    No fish died during anaesthesia. During the entire study, there were no discernible differences in the swimming behaviour of exposed fish and control fish. No gross changes were observed in the livers of the control fish; the liver was reddish brown and had tender structure. In contrast, the enlarged liver of the MC-LR-challenged fish was readily apparent throughout the whole exposure period. At 8 h post-injection, the livers were slightly redder than these from the control group. However, a progressive development of discoloration of this organ was observed after 24 and 48 h of the exposure . In some cases, the liver structure of the exposed fish was partially liquefied.

(a)

Control 0 h   Exposed 8 h
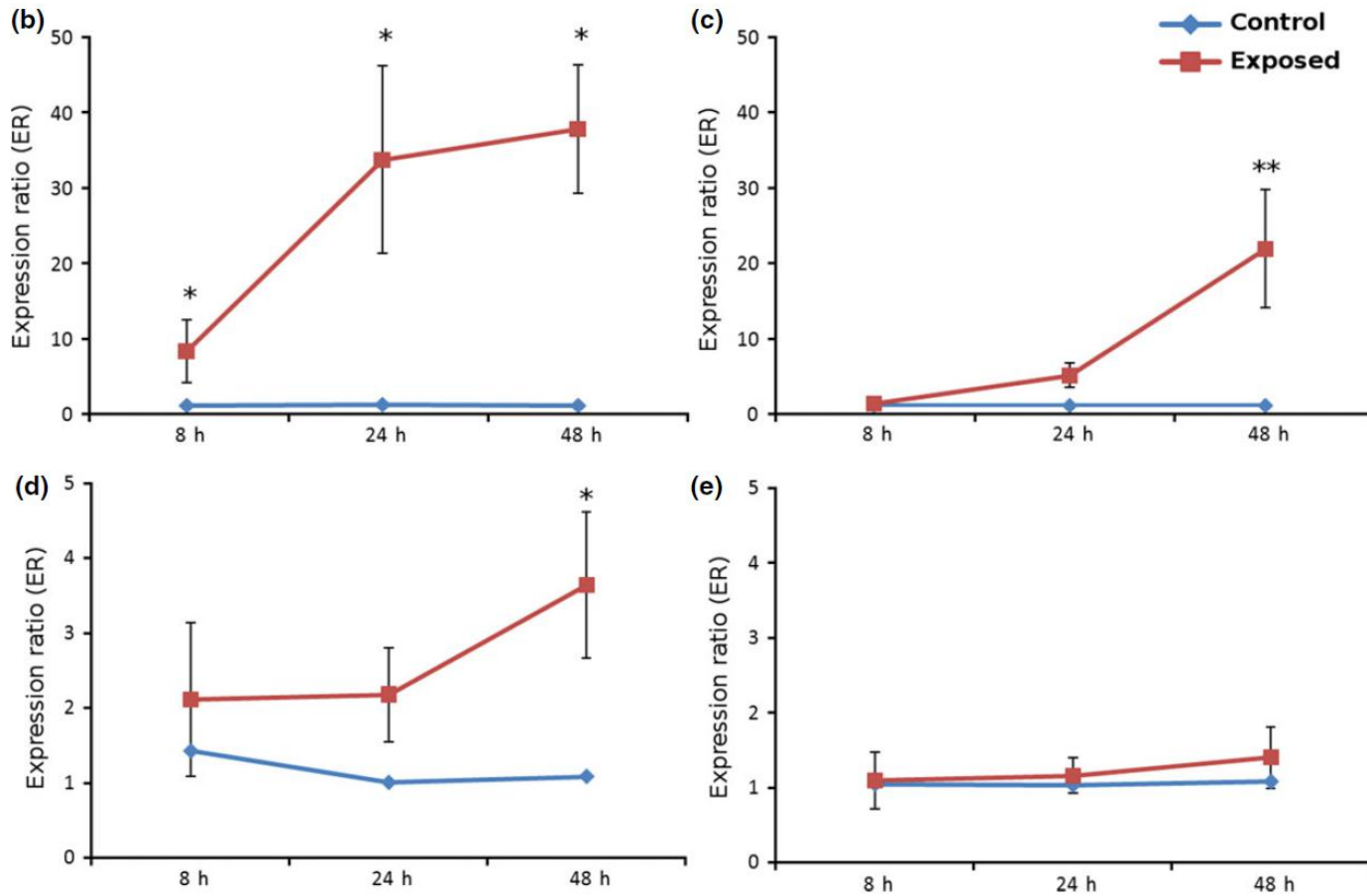
Exposed 24 h   Exposed 48 h

Figure 1 Gross appearance of whitefish liver and changes in plasma levels of four miRNA examined in the study.(b) miR-122-5p, (c) miR-148a-3p, (d) miR-92a-3p and (e) let-7c-5p

结果和分析

Markers represent mean values (n = 5, except for control sample at 24 h and 48 h where n = 3) of expression ratios (R $\pm$SE), normalized by cel-miR-39-3p as reference microRNA at each respective time of the experiment. Data were analysed using REST 2009 software. Asterisks denote exposure group means that are significantly different from control group using a randomization test.

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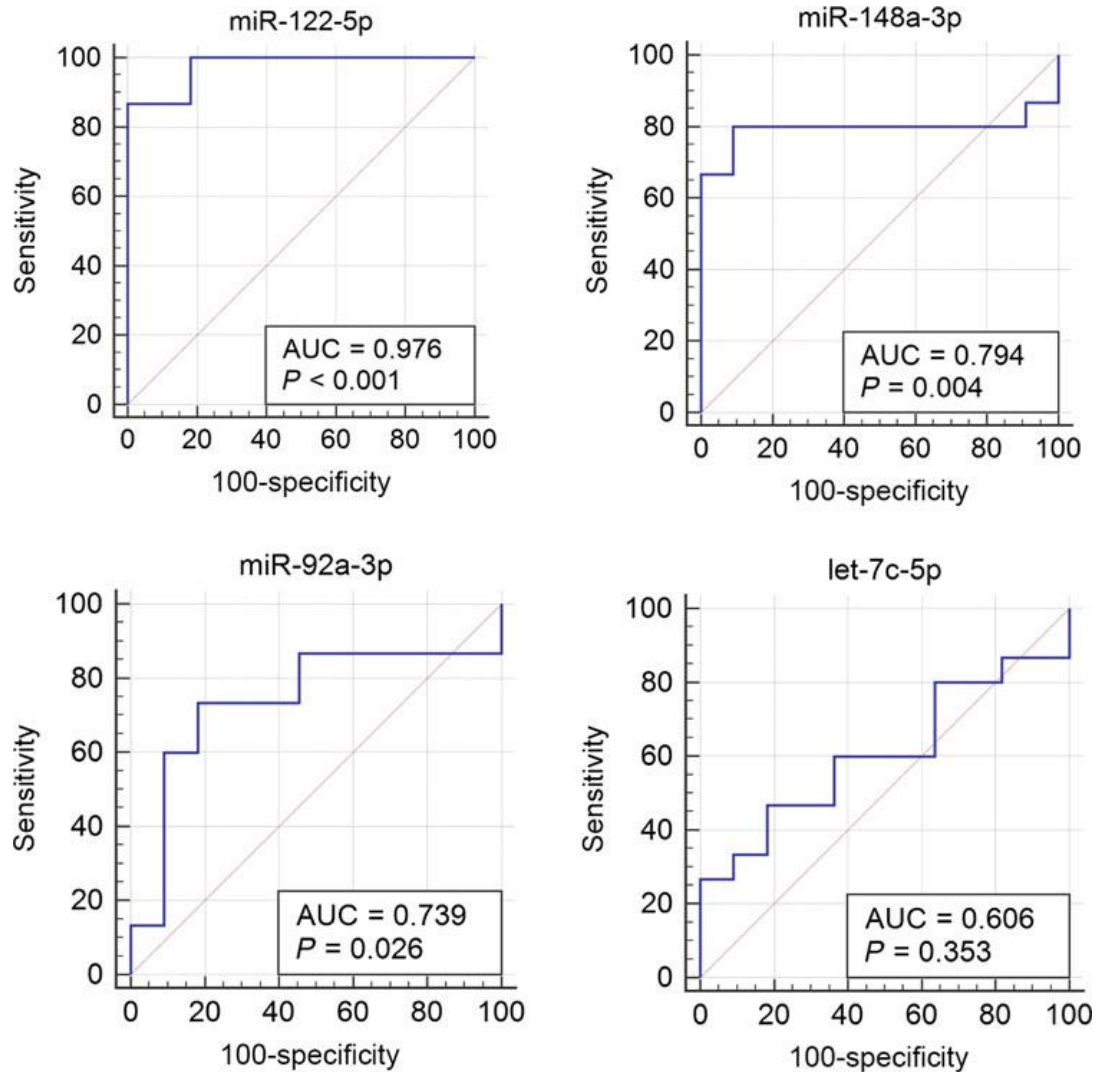【分享】real time PCR数据分析 REST2009软件及其使用说明

Figure 2 Receiver operating characteristics (ROC) analysis of serum miRNAs as liver injury risk biomarkers in whitefish exposed to MC-LR.

ROC曲线评价统计量计算。ROC曲线下的面积值在1.0和0.5之间。在AUC>0.5的情况下，AUC越接近于1，说明诊断效果越好。AUC在0.5～0.7时有较低准确性，AUC在0.7～0.9时有一定准确性，AUC在0.9以上时有较高准确性。AUC=0.5时，说明诊断方法完全不起作用，无诊断价值。AUC<0.5不符合真实情况，在实际中极少出现。

The ROC curve analysis was conducted with MedCalc Statistical software version 15.2 (MedCalc software bvba; http://www.medcalc.org; 2015).
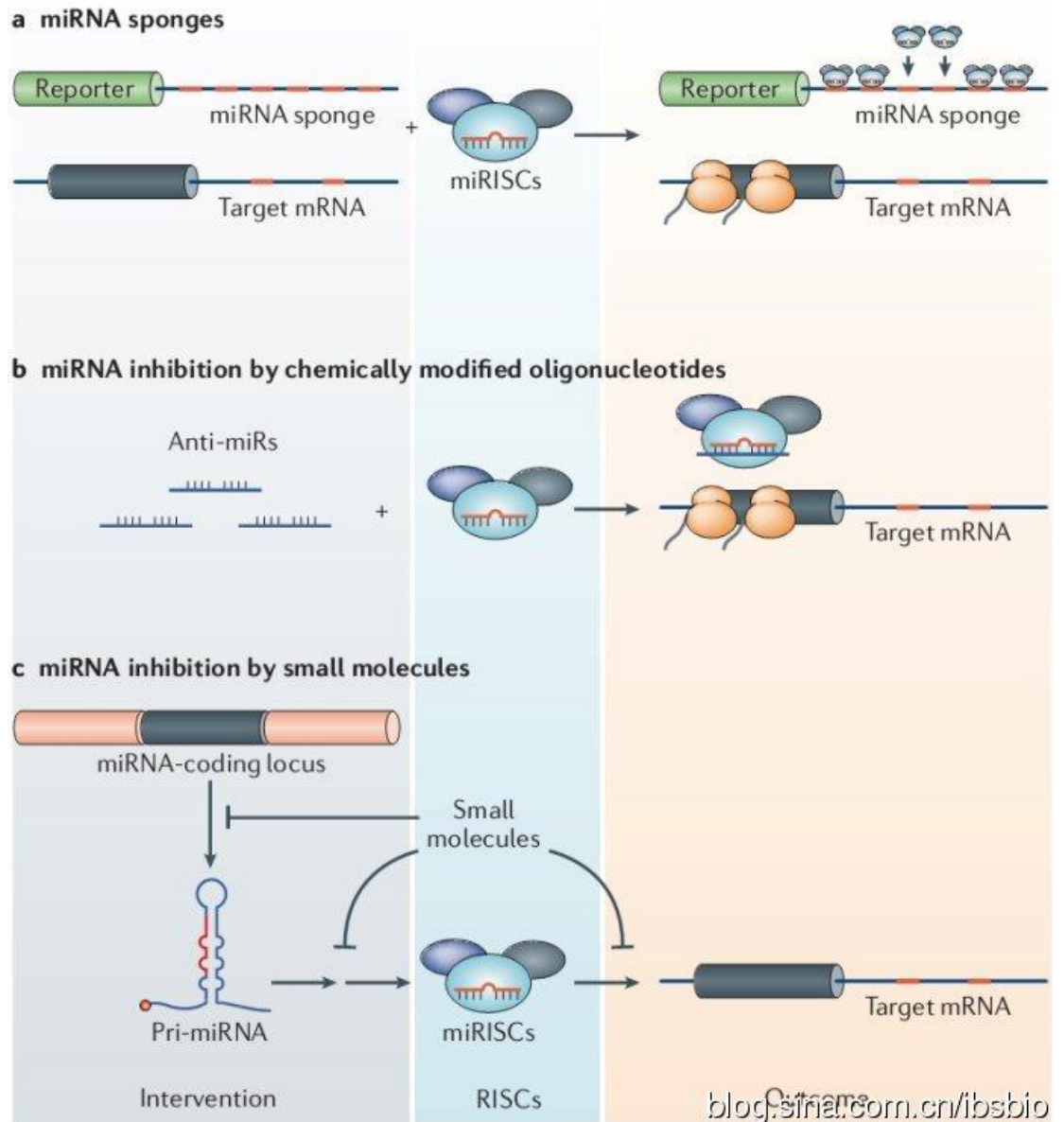
结果和分析

小结

    To sum up, the results of our study suggest that miRNA-122 can be used in environmental studies as a non-invasive biomarker to detect liver damage in fish, as a promising alternative to today's gold standard hepatotoxicity markers. **Plasma levels of miRNA-122-5p in whitefish** are elevated within 8 h of exposure to MC-LR and show high specificity, with an AUC value of 0.976 (P < 0.001).miR-148a-3p and miR-92a-3p, although they respond more slowly to exposure to MC-LR and have lower AUC values, also show potential and are worth further investigating.

思考与感悟

1. miR-122与肝脏脂质代谢研究

a miRNA sponges

b miRNA inhibition by chemically modified oligonucleotides

c miRNA inhibition by small molecules

思考与感悟

2.注射后鱼类行为状态观察

THANKS