AU-1

## ELENCHI DI QUESITI PREDISPOSTI PER COLLOQUIO

---

### Elenco 1

**Domanda 1A**: Quali parametri ritiene rilevanti nel pesare l'impatto e nel calcolare il contributo di ogni utilizzatore di un lab multiutenza a riguardo? Come pensa di gestire il problema dal punto di vista informatico?

**Domanda 1B**: Quali batteri e virus patogeni potrebbero essere rilevati in uno stabulario di topi e quali strategie si potrebbero adottare di conseguenza?

**Domanda 1C**: Se, incrociando topi transgenici, venisse rilevata nella progenie una contaminazione da transgene non previsto, come risolverebbe il problema?

**Accertamento informatico:** Principali caratteristiche ed usi del pacchetto Microsoft Office in un laboratorio di ricerca.

---

### Elenco 2

**Domanda 2A**: Quali tipologie di servizio eroga un lab manager di un laboratorio multiutenza e come potrebbero essere gestite amministrativamente le richieste di ordini e reagenti?

**Domanda 2B**: Qual è la vita media di uno topo (riproduttiva e totale) e quali strategie si possono adottare per la gestione dell'invecchiamento degli stock?

**Domanda 2C**: Se in una gabbia di topi dentro un singolo rack si verificasse una moria generalizzata, quali strategie metterebbe in atto?

**Accertamento informatico:** Principali caratteristiche ed usi del °Cloud° e suite di software in un laboratorio di ricerca.

---

### Elenco 3

**Domanda 3A**: Quali strategie di tipo informatico si potrebbero adottare per fornire un accesso rapido alle informazioni di tipo sperimentale (reagenti, linee animali, protocolli) agli utenti di un laboratorio multiutenza?

**Domanda 3B**: Quali informazioni essenziali vanno comunicate in un corso introduttivo per nuovi afferenti ad un laboratorio multiutenza e con quali modalità accerterebbe l'apprendimento?

**Domanda 3C**: Una linea di topi mantenuta viva ha raggiunto un livello critico (solo 1 topo sopravvissuto); quali strategie metterebbe in atto per ri-espandere la linea e per evitare problemi in futuro?

**Accertamento informatico:** Principali caratteristiche ed usi di piattaforme come Google Suite o simili in un laboratorio di ricerca.

Amino Acids (2016) 48:2549–2558
DOI 10.1007/s00726-016-2278-0

ORIGINAL ARTICLE

# Glycine inhibits angiogenesis in colorectal cancer: role of endothelial cells

**Helge Bruns[1] · Darius Kazanavicius[1,2] · Daniel Schultze[1] · Mohammed Al Saeedi[1] · Kenia Yamanaka[1] · Kestutis Strupas[2] · Peter Schemmer[1]**

Received: 7 October 2015 / Accepted: 10 June 2016 / Published online: 28 June 2016


**Abstract** Neo-angiogenesis is important for tumor growth. Glycine is a non-toxic amino acid with suspected anti-angiogenic effects. This study was designed to evaluate anti-angiogenic effects of glycine in colorectal cancer. Glycine was added to cultures of human and rat colorectal cancer cells (CRC), and endothelial cells (HUVEC). Glycine's direct impact was monitored using MTT assays. Angiogenesis in HUVEC was monitored using 3D sprouting and migration assays. VEGF and CRC-conditioned media were used to stimulate angiogenesis. The glycine receptor (GlyR) was detected using Western blotting and inhibited using strychnine. The WAG-Rij/CC-531 model of metastatic CRC was used to evaluate glycine's impact in vivo. Tumor growth and vessel density were monitored in rats fed with or without 5 % glycine for 14 days. VEGF and conditioned media significantly increased proliferation, migration, and capillary formation to up to 267 %. Glycine completely neutralized this effect and strychnine completely blunted glycine's effect. GlyR was detected in HUVEC. Tumor volume, weight, and vessel density decreased by 35 % ($p = 0.02$), 34 % ($p = 0.03$), and 55 % ($p = 0.04$) in glycine-fed animals. Glycine inhibits angiogenic signaling of endothelial cells and tumor growth. Glycine would be a promising additive to standard and targeted cancer therapies.

**Keywords** Angiogenesis inhibitors · Colorectal neoplasia · Endothelial cells · Glycine

Handling Editor: G. J. Peters.

H. Bruns and D. Kazanavicius contributed equally to this work.

✉ Peter Schemmer
Peter.Schemmer@med.uni-heidelberg.de

[1] Department of General, Visceral and Transplant Surgery, University Hospital Heidelberg, Im Neuenheimer Feld 110, 69120 Heidelberg, Germany

[2] Center of Abdominal Surgery, Vilnius University Hospital Santariskiu Klinikos, Vilnius, Lithuania

## Introduction

Colorectal cancer (CRC) is one of the leading causes of cancer related deaths (Center et al. 2009a, b; Jemal et al. 2011). In almost 50 % of patients, tumors are in an advanced stage with metastases. Multifaceted treatment regimens usually combine surgery and (neo-)adjuvant chemotherapy techniques, in combination with targeted therapies using antibodies and kinase inhibitors, and have led to dramatically prolonged survival (Prenen et al. 2013; Loupakis et al. 2014; Folprecht 2010; Folprecht et al. 2010; Papa et al. 2012; Stremitzer et al. 2012; Zani et al. 2013). Although modern therapy is often curative, the available treatments are still limited and may not be successful in all patients. In advanced and metastatic diseases, tumor recurrence and the detection of previously unknown metastases are frequent (Bouviez et al. 2014; Tan et al. 2013; Young et al. 2014). Cancer cells can escape targeted therapies and can eventually become resistant to known therapies (Koido et al. 2013). As such, there is a desperate need for the identification of chemo-additive treatments with low toxicity to further improve survival, especially in those cases where no curative therapy approach is available.

Angiogenesis is one of the essential steps in the growth and progression of cancer (Hanahan and Weinberg 2000, 2011). Without neovascularization, tumors